


AstraZeneca
AstraZeneca PLC
(incorporated with limited liability in England)

US\$10,000,000,000
Euro Medium Term Note Programme

AstraZeneca PLC (the "**Issuer**") has established a Euro Medium Term Note Programme (the "**Programme**") described in this Base Prospectus. Pursuant to the Programme, the Issuer may from time to time issue notes ("**Notes**") up to the maximum aggregate principal amount of US\$10,000,000,000.

Notes will be issued in series (each a "**Series**") in bearer form. Each Series may comprise one or more tranches (each a "**Tranche**") issued on different issue dates. Each Tranche of Notes will be issued on the terms set out herein under "*Terms and Conditions of the Notes*" (the "**Conditions**") as completed by a document setting out the final terms of such Tranche (the "**Final Terms**") or as amended, supplemented and/or replaced in a separate prospectus specific to such Tranche (the "**Drawdown Prospectus**") as described under "*Final Terms and Drawdown Prospectuses*" below. In the case of a Tranche of Notes which is the subject of a Drawdown Prospectus, each reference in this Base Prospectus to information being specified or identified in the relevant Final Terms shall be read and construed as a reference to such information being specified or identified in the relevant Drawdown Prospectus unless the context requires otherwise. This Base Prospectus must be read and construed together with all documents incorporated by reference herein, any amendments or supplements hereto and, in relation to any Tranche of Notes which is the subject of Final Terms, must be read and construed together with the relevant Final Terms.

The Notes are constituted by, have the benefit of and are in all respects subject to a trust deed dated 10 September 2007 and amended and restated on 12 June 2019 (the "**Trust Deed**") between the Issuer and Deutsche Trustee Company Limited (the "**Trustee**", which expression shall include all persons appointed for the time being as trustee or trustees under the Trust Deed) as trustee for the holders of the Notes (the "**Noteholders**"). The Notes also have the benefit of an amended and restated agency agreement dated 12 June 2019 (the "**Agency Agreement**") between the Issuer, Deutsche Bank AG, London Branch as principal paying agent (the "**Principal Paying Agent**") and Deutsche Bank AG, Hong Kong Branch as CMU lodging and paying agent (the "**CMU Lodging and Paying Agent**").

This Base Prospectus has been approved by the United Kingdom Financial Conduct Authority (the "**FCA**"), which is the United Kingdom competent authority for the purposes of Directive 2003/71/EC, as amended or superseded, and as implemented by any relevant implementing measures in the United Kingdom (the "**Prospectus Directive**"), as a base prospectus issued in compliance with the Prospectus Directive for the purpose of giving information with regard to the issue of Notes issued under the Programme described in this Base Prospectus during the period of twelve months after the date hereof. Applications have been made for the Notes to be admitted to listing on the Official List of the FCA and to trading on the Regulated Market of the London Stock Exchange plc (the "**London Stock Exchange**") during the period of twelve months after the date hereof. The Regulated Market of the London Stock Exchange is a regulated market for the purposes of Directive 2014/64/EU on markets in financial instruments (as amended, "**MiFID II**").

The Notes are to be admitted to trading on a market which is a regulated market for the purposes of the MiFID II (each a "**Regulated Market**") and offered to the public in any Member State of the European Economic Area and may only be issued under the Programme in minimum denominations of at least EUR 100,000 (or its equivalent in another currency).

Investing in Notes issued under the Programme involves certain risks. The principal risk factors that may affect the ability of the Issuer to fulfil its obligations under the Notes are discussed under "Risk Factors" below.

Arranger

CITIGROUP

Dealers

BARCLAYS
CITIGROUP
GOLDMAN SACHS INTERNATIONAL
J.P. MORGAN CAZENOVE

BoFA MERRILL LYNCH
DEUTSCHE BANK
HSBC
MIZUHO SECURITIES

MORGAN STANLEY

The date of this Base Prospectus is 12 June 2019

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IMPORTANT NOTICES

The Issuer accepts responsibility for the information contained in this Base Prospectus and declares that, having taken all reasonable care to ensure that such is the case, the information contained in this Base Prospectus is, to the best of its knowledge, in accordance with the facts and contains no omission likely to affect its import.

No person has been authorised to give any information or to make any representation not contained in or not consistent with this Base Prospectus or any other document entered into in relation to the Programme or any information supplied by the Issuer or such other information as is in the public domain and, if given or made, such information or representation should not be relied upon as having been authorised by the Issuer, the Trustee or any Dealer.

Neither the Dealers nor any of their respective affiliates nor the Agents or the Trustee have authorised the whole or any part of this Base Prospectus and none of them makes any representation or warranty or accepts any responsibility as to the accuracy or completeness of the information contained in this Base Prospectus. Neither the delivery of this Base Prospectus or any Final Terms nor the offering, sale or delivery of any Note shall, in any circumstances, create any implication that the information contained in this Base Prospectus is true subsequent to the date hereof or the date upon which this Base Prospectus has been most recently amended or supplemented or that there has been no adverse change, or any event reasonably likely to involve any adverse change, in the prospects or financial or trading position of the Issuer since the date thereof or, the date upon which this Base Prospectus has been most recently amended or supplemented or that any other information supplied in connection with the Programme is correct at any time subsequent to the date on which it is supplied or, if different, the date indicated in the document containing the same.

The distribution of this Base Prospectus and any Final Terms and the offering, sale and delivery of the Notes in certain jurisdictions may be restricted by law. Persons into whose possession this Base Prospectus or any Final Terms comes are required by the Issuer and the Dealers to inform themselves about and to observe any such restrictions. For a description of certain restrictions on offers, sales and deliveries of Notes and on the distribution of this Base Prospectus or any Final Terms and other offering material relating to the Notes, see "*Subscription and Sale*". In particular, Notes have not been and will not be registered under the United States Securities Act of 1933 (as amended) (the "**Securities Act**") and are subject to U.S. tax law requirements. Subject to certain exceptions, Notes may not be offered, sold or delivered within the United States or to U.S. persons.

Neither this Base Prospectus nor any Final Terms constitutes an offer or an invitation to subscribe for or purchase any Notes and should not be considered as a recommendation by the Issuer, the Dealers or any of them that any recipient of this Base Prospectus or any Final Terms should subscribe for or purchase any Notes. Each recipient of this Base Prospectus or any Final Terms shall be taken to have made its own investigation and appraisal of the condition (financial or otherwise) of the Issuer.

The maximum aggregate principal amount of Notes outstanding at any one time under the Programme will not exceed US\$10,000,000,000 (and for this purpose, any Notes denominated in another currency shall be translated into U.S. dollars at the date of the agreement to issue such Notes (calculated in accordance with the provisions of the Dealer Agreement)). The maximum aggregate principal amount of Notes which may be outstanding at any one time under the Programme may be increased from time to time, subject to compliance with the relevant provisions of the Dealer Agreement as defined under "*Subscription and Sale*".

The Programme has been rated by S&P Global Ratings Europe Limited, UK Branch ("**S&P**") and by Moody's France SAS ("**Moody's**"), as more fully set out in "*Description of the Programme*" below, which are established in the European Economic Area (the "**EEA**") and registered under Regulation (EU) No 1060/2009, as amended (the "**CRA Regulation**"). As such, Moody's and S&P are included in the list of registered credit rating agencies published by the European Securities and Markets Authority ("**ESMA**") on its website in accordance with such Regulation at www.esma.europa.eu/page/List-registered-and-certified-CRAs (list last updated as of 18 March 2019).

Tranches of Notes issued under the Programme may be rated or unrated. Where a Tranche of Notes is rated, such rating will not necessarily be the same as the ratings assigned to the Programme as described above or the rating(s) assigned to Notes already issued. Where a Tranche of Notes is rated, the applicable rating(s) will be specified in the relevant Final Terms. Whether or not each credit rating applied for in relation to a relevant Tranche of Notes will be (1) issued by a credit rating agency established in the EEA and registered under the CRA Regulation, or (2) issued by a credit rating agency which is not established in the EEA but will be

endorsed by a CRA which is established in the EEA and registered under the CRA Regulation or (3) issued by a credit rating agency which is not established in the EEA but which is certified under the CRA Regulation will be disclosed in the Final Terms.

In general, European regulated investors are restricted from using a rating for regulatory purposes if such rating is not issued by a credit rating agency established in the EEA and registered under the CRA Regulation unless (1) the rating is provided by a credit rating agency not established in the EEA but is endorsed by a credit rating agency established in the EEA and registered under the CRA Regulation or (2) the rating is provided by a credit rating agency not established in the EEA which is certified under the CRA Regulation.

A security rating is not a recommendation to buy, sell or hold securities and may be subject to suspension, reduction or withdrawal at any time by the assigning rating agency.

Each potential investor in the Notes must determine the suitability of that investment in light of its own circumstances. In particular, each potential investor should:

- (a) have sufficient knowledge and experience to make a meaningful evaluation of the Notes and the merits and risks of investing in the Notes on the basis of the information contained or incorporated by reference in this Base Prospectus or any applicable supplement;
- (b) have access to, and knowledge of, appropriate analytical tools to evaluate, in the context of its particular financial situation, an investment in the Notes and the impact the Notes will have on its overall investment portfolio;
- (c) have sufficient financial resources and liquidity to bear all of the risks of an investment in the Notes, including Notes with principal or interest payable in one or more currencies, or where the currency for principal or interest payments is different from the potential investor's currency;
- (d) understand thoroughly the terms of the Notes and be familiar with the behaviour of any relevant indices and financial markets; and
- (e) be able to evaluate (either alone or with the help of a financial adviser) possible scenarios for economic, interest rate and other factors that may affect its investment and its ability to bear the applicable risks.

The investment activities of certain investors are subject to legal investment laws and regulations, or review or regulation by certain authorities. Each potential investor should consult its legal advisers to determine whether and to what extent (1) Notes are legal investments for it, (2) Notes can be used as collateral for various types of borrowing and (3) other restrictions apply to its purchase or pledge of any Notes. Financial institutions should consult their legal advisers or the appropriate regulators to determine the appropriate treatment of Notes under any applicable risk-based capital or similar rules.

In this Base Prospectus, unless otherwise specified, references to a "**Member State**" are references to a Member State of the EEA, references to "**US\$**", "**U.S. dollars**" or "**dollars**" are to United States dollars, references to "**EUR**" or "**euro**" are to the single currency introduced at the start of the third stage of European Economic and Monetary Union, and as defined in Article 2 of Council Regulation (EC) No. 974/98 of 3 May 1998 on the introduction of the euro, as amended, references to "**£**" or "**sterling**" are to the lawful currency for the time being of the United Kingdom and references to "**Renminbi**", "**Chinese Yuan**", "**CNY**" and "**RMB**" are to the lawful currency of the People's Republic of China (for the purpose of this Base Prospectus, excluding the Hong Kong Special Administrative Region, the Macau Special Administrative Region and Taiwan) ("**PRC**").

Certain figures included in this Base Prospectus have been subject to rounding adjustments; accordingly, figures shown for the same category presented in different tables may vary slightly and figures shown as totals in certain tables may not be an arithmetic aggregation of the figures which precede them. All figures included in this Base Prospectus which express growth rates are expressed at constant exchange rates unless otherwise stated.

In connection with the issue of any Tranche of Notes, the Dealer or Dealers (if any) acting as the Stabilisation Manager(s) (or persons acting on behalf of any Stabilisation Manager(s)) may over allot Notes or effect transactions with a view to supporting the market price of the Notes at a level higher than that which might otherwise prevail. However, stabilisation may not necessarily occur. Any stabilisation action may begin on or after the date on which adequate public disclosure of the terms of the offer of the

relevant Tranche of Notes is made and, if begun, may cease at any time, but it must end no later than the earlier of 30 days after the issue date of the relevant Tranche of Notes and 60 days after the date of the allotment of the relevant Tranche of Notes. Any stabilisation action or over-allotment must be conducted by the relevant Stabilisation Manager(s) (or persons acting on behalf of any Stabilisation Manager(s)) in accordance with all applicable laws and rules.

IMPORTANT EEA RETAIL INVESTORS

If the relevant Final Terms in respect of any Notes includes a legend entitled "Prohibition of Sales to EEA Retail Investors", the Notes are not intended to be offered, sold or otherwise made available to, and should not be offered, sold or otherwise made available to any retail investor in the EEA. For these purposes, a retail investor means a person who is one (or more) of: (i) a retail client as defined in point (11) of Article 4(1) of MiFID II; or (ii) a customer within the meaning of Directive 2002/92/EC, as amended or superseded, where that customer would not qualify as a professional client as defined in point (10) of Article 4(1) of MiFID II. Consequently no key information document required by Regulation (EU) No. 1286/2014 (the "**PRIIPs Regulation**") for offering or selling the Notes or otherwise making them available to retail investors in the EEA has been prepared and therefore offering or selling the Notes or otherwise making them available to any retail investor in the EEA may be unlawful under the PRIIPs Regulation.

MIFID II PRODUCT GOVERNANCE/TARGET MARKETS

The Final Terms (as defined below) in respect of any Notes will include a legend entitled "MiFID II Product Governance" which will outline the target market assessment in respect of the Notes and which channels for distribution of the Notes are appropriate. Any person subsequently offering, selling or recommending the Notes (a "**distributor**") should take into consideration the target market assessment; however, a distributor subject to MiFID II is responsible for undertaking its own target market assessment in respect of the Notes (by either adopting or refining the target market assessment) and determining appropriate distribution channels.

A determination will be made in relation to each issue of Notes about whether, for the purpose of the MiFID Product Governance rules under EU Delegated Directive 2017/593 (the "**MiFID Product Governance Rules**"), any Dealer subscribing for any Notes is a manufacturer in respect of such Notes, but otherwise neither the Arranger nor the Dealers nor any of their respective affiliates will be a manufacturer for the purpose of the MiFID Product Governance Rules.

BENCHMARK REGULATION

Interest and/or other amounts payable under the Notes may be calculated by reference to certain reference rates. Any such reference rate may constitute a benchmark for the purposes of Regulation (EU) 2016/1011 (the "**Benchmark Regulation**"). If any such reference rate does constitute such a benchmark, the Final Terms will indicate whether or not the benchmark is provided by an administrator included in the register of administrators and benchmarks established and maintained by ESMA pursuant to Article 36 (*Register of administrators and benchmarks*) of the Benchmark Regulation. Transitional provisions in the Benchmark Regulation may have the result that the administrator of a particular benchmark is not required to appear in the register of administrators and benchmarks at the date of the Final Terms. The registration status of any administrator under the Benchmark Regulation is a matter of public record and, save where required by applicable law, the Issuer does not intend to update the Final Terms to reflect any change in the registration status of the administrator.

PRODUCT CLASSIFICATION PURSUANT TO SECTION 309B OF THE SECURITIES AND FUTURES ACT (CHAPTER 289 OF SINGAPORE)

The Final Terms in respect of any Notes may include a legend entitled "**Singapore Securities and Futures Act Product Classification**" which will state the product classification of the Notes pursuant to section 309B(1) of the Securities and Futures Act (Chapter 289 of Singapore) (the "**SFA**"). The Issuer will make a determination in relation to each issue about the classification of the Notes being offered for the purposes of section 309B(1)(a). Any such legend included on the relevant Final Terms will constitute notice to "relevant persons" for the purposes of section 309B(1)(c) of the SFA.

DESCRIPTION OF THE PROGRAMME

This description of the Programme must be read as an introduction to this Base Prospectus, and any decision to invest in the Notes should be based on a consideration of the Base Prospectus as a whole, including all documents incorporated by reference. Words and expressions defined in the "Terms and Conditions of the Notes" below or elsewhere in this Base Prospectus have the same meanings in this summary.

Issuer:	AstraZeneca PLC.
Risk Factors:	Investing in Notes issued under the Programme involves certain risks. The principal risk factors that may affect the ability of the Issuer to fulfil their respective obligations under the Notes are discussed under " <i>Risk Factors</i> " below.
Arranger:	Citigroup Global Markets Limited.
Dealers:	Barclays Bank PLC, Citigroup Global Markets Limited, Deutsche Bank AG, London Branch, Goldman Sachs International, HSBC Bank plc, J.P. Morgan Securities plc, Merrill Lynch International, Mizuho International plc, Morgan Stanley & Co. International plc and any other Dealer appointed from time to time by the Issuer either generally in respect of the Programme or in relation to a particular Tranche of Notes.
Trustee:	Deutsche Trustee Company Limited.
Principal Paying Agent:	Deutsche Bank AG, London Branch.
CMU Lodging and Paying Agent:	Deutsche Bank AG, Hong Kong Branch.
Final Terms or Drawdown Prospectus:	Notes issued under the Programme may be issued either (1) pursuant to this Base Prospectus and associated Final Terms or (2) pursuant to a Drawdown Prospectus. The terms and conditions applicable to any particular Tranche of Notes will be the Terms and Conditions of the Notes as completed by the relevant Final Terms or, as the case may be, as supplemented, amended and/or replaced to the extent described in the relevant Drawdown Prospectus.
Listing and Trading:	Application has been made for Notes to be admitted during the period of twelve months after the date hereof to listing on the Official List of the FCA and to trading on the Regulated Market of the London Stock Exchange.
Clearing Systems:	Euroclear and/or Clearstream or CMU, in relation to any Tranche of Notes.
Initial Programme Amount:	Up to US\$10,000,000,000 (or its equivalent in other currencies) aggregate principal amount of Notes outstanding at any one time. The Issuer may increase the amount of the Programme at any time, subject to compliance with the relevant provisions of the Dealer Agreement as defined under " <i>Subscription and Sale</i> ".
Issuance in Series:	Notes will be issued in Series. Each Series may comprise one or more Tranches issued on different issue dates. The Notes of each Series will all be subject to identical terms, except that the issue date, issue price and the amount of the first payment of interest may be different in respect of different Tranches.
Forms of Notes:	Notes may only be issued in bearer form. Each Tranche of Notes will initially be in the form of either a Temporary Global Note or a Permanent Global Note, in each case as specified in the relevant Final Terms. Each Global Note which is not intended to be issued in new

global note form (a "**Classic Global Note**" or "**CGN**"), as specified in the relevant Final Terms, will be deposited on or around the relevant issue date with a depositary or a common depositary for Euroclear and/or Clearstream and/or lodged with a sub-custodian for CMU and/or any other relevant clearing system and each Global Note which is intended to be issued in new global note form (a "**New Global Note**" or "**NGN**"), as specified in the relevant Final Terms, will be deposited on or around the relevant issue date with a common safekeeper for Euroclear and/or Clearstream. Each Temporary Global Note will be exchangeable for a Permanent Global Note or, if so specified in the relevant Final Terms, for Definitive Notes. If the TEFRA D Rules are specified in the relevant Final Terms as applicable, certification as to non-U.S. beneficial ownership will be a condition precedent to any exchange of an interest in a Temporary Global Note or receipt of any payment of interest in respect of a Temporary Global Note. Each Permanent Global Note will be exchangeable for Definitive Notes in accordance with its terms. Definitive Notes will, if interest-bearing, have Coupons attached and, if appropriate, a Talon for further Coupons.

- Currencies:** Notes may be denominated in any currency or currencies, subject to compliance with all applicable legal and/or regulatory and/or central bank requirements. Payments in respect of Notes may, subject to such compliance, be made in and/or linked to, any currency or currencies other than the currency in which such Notes are denominated.
- Status of the Notes:** Notes will be issued on an unsubordinated basis.
- Issue Price:** Notes may be issued at any price, as specified in the relevant Final Terms. The price and amount of Notes to be issued under the Programme will be determined by the Issuer and the relevant Dealer(s) at the time of issue in accordance with prevailing market conditions.
- Maturities:** Such maturity as may be agreed between the Issuer and the relevant Dealer(s), subject to such minimum or maximum maturities as may be allowed or required from time to time by the Bank of England (or equivalent body) or any laws or regulations applicable to the Issuer or the relevant currency.
- Any Notes having a maturity of less than one year must (a) have a minimum redemption value of £100,000 (or its equivalent in other currencies) and be issued only to persons whose ordinary activities involve them in acquiring, holding, managing or disposing of investments (as principal or agent) for the purposes of their businesses; or who it is reasonable to expect will acquire, hold, manage or dispose of investments (as principal or agent) for the purposes of their businesses or (b) be issued in other circumstances which do not constitute a contravention of section 19 of the Financial Services and Markets Act 2000, as amended (the "**FSMA**") by the Issuer.
- Redemption:** Notes may be redeemable at par or at such other redemption amount as may be specified in the relevant Final Terms.
- Optional Redemption:** Notes may be redeemed before their stated maturity at the option of the Issuer (either in whole or in part) and/or at the option of the Noteholders to the extent (if at all) specified in the relevant Final Terms.
- Tax Redemption:** Except as described in "*Optional Redemption*" above, early redemption will only be permitted for tax reasons as described in Condition 9(b) (*Redemption and Purchase — Redemption for tax reasons*).

Interest:	Notes may be interest-bearing or non-interest bearing. Interest (if any) may accrue at a fixed rate or a floating rate or other variable rate and the method of calculating interest may vary between the issue date and the maturity date of the relevant Series. For the avoidance of doubt, the interest rate in respect of floating rate Notes shall not be less than zero.
Denominations:	No Notes may be issued under the Programme with a minimum denomination of less than EUR 100,000. Notes will be issued in such denominations as may be specified in the relevant Final Terms, subject to compliance with all applicable legal and/or regulatory and/or central bank requirements.
Negative Pledge:	The Notes will have the benefit of a negative pledge as described in Condition 5 (<i>Negative Pledge</i>).
Taxation:	All payments in respect of Notes will be made free and clear of withholding taxes of the United Kingdom, unless the withholding is required by law. In that event, the Issuer will (subject as provided in Condition 11 (<i>Taxation</i>)) pay such additional amounts as will result in the Noteholders receiving such amounts as they would have received in respect of such Notes had no such withholding been required.
Governing Law:	The Notes and the Trust Deed and any non-contractual obligations arising out of or in connection with the Notes and the Trust Deed are governed by English law.
Ratings:	<p>The Programme has been rated as follows by S&P and by Moody's which are established in the EEA and registered under the CRA Regulation:</p> <p>S&P Global Ratings Europe Limited, UK Branch: BBB+</p> <p>Moody's France SAS: A3</p> <p>Notes issued under the Programme may be rated or unrated. Where an issue of Notes is rated, its rating will not necessarily be the same as the rating assigned to the Programme as described above or the rating(s) assigned to Notes already issued. A rating is not a recommendation to buy, sell or hold securities and may be subject to suspension, change or withdrawal at any time by the assigning rating agency.</p> <p>In general, European regulated investors are restricted from using a rating for regulatory purposes if such rating is not issued by a credit rating agency established in the EEA and registered under the CRA Regulation unless (1) the rating is provided by a credit rating agency not established in the EEA but is endorsed by a credit rating agency established in the EEA and registered under the CRA Regulation or (2) the rating is provided by a credit rating agency not established in the EEA which is certified under the CRA Regulation.</p>
Selling Restrictions:	For a description of certain restrictions on offers, sales and deliveries of Notes and on the distribution of offering material in the United States of America, the EEA, the United Kingdom, Japan, the People's Republic of China, Hong Kong and Singapore see " <i>Subscription and Sale</i> " section on page 104.

RISK FACTORS

Prospective investors should read the entire Base Prospectus. Words and expressions defined in the "Terms and Conditions of the Notes" below or elsewhere in this Base Prospectus have the same meanings in this section.

Investing in Notes issued under the Programme involves certain risks. Set forth below are risk factors that the Issuer believes are the principal risks involved in an investment in the Notes. Prospective investors should consider carefully the following:

RISKS RELATING TO FORWARD-LOOKING STATEMENTS

This Base Prospectus contains certain forward-looking statements about the Issuer. The Issuer believes such forward-looking statements, identified by words such as 'anticipates', 'believes', 'expects' and 'intends', are based on reasonable assumptions. However, forward-looking statements involve inherent risks and uncertainties such as those summarised below. They relate to events that may occur in the future, that may be influenced by factors beyond the Issuer's control and that may have actual outcomes materially different from the Issuer's expectations.

RISKS RELATING TO THE ISSUER AND ITS BUSINESS

The pharmaceutical sector is inherently risky and a variety of risks and uncertainties may affect the Issuer's business. Here the Issuer summarises, under the headings Product Pipeline and Intellectual Property Risks; Commercialisation Risks; Supply Chain and Business Execution Risks; Legal, Regulatory and Compliance Risks; and Economic and Financial Risks, the principal risks and uncertainties that it currently considers may have a significant effect on its financial condition, results of operations and/or reputation. These risks are not listed in any assumed order of priority. Other risks, unknown or not currently considered material, could have a similar effect.

Product Pipeline and Intellectual Property Risks

Failure or delay in delivery of pipeline or launch of new products

The Issuer's continued success depends on the development and successful launch of innovative new drugs.

The development of pharmaceutical product candidates is a complex, risky and lengthy process involving significant financial, research and development ("R&D") and other resources. A project may fail at any stage of the process due to various factors, including failure to obtain the required regulatory or marketing approvals for the product candidate or for its manufacturing facilities, unfavourable clinical efficacy data, safety concerns, failure to demonstrate adequate cost-effective benefits to regulatory authorities and/or payers and the emergence of competing products.

The anticipated launch dates of major new products significantly affect the Issuer's business, including investment in large clinical studies, the manufacture of pre-launch product stocks, investment in marketing materials pre-launch, sales force training and the timing of anticipated future revenue streams from new product sales. Launch dates are primarily driven by the Issuer's development programmes and various other factors, including findings in pre-clinical or clinical studies, regulatory demands, price negotiation, competitor activity and technology transfer. More complex and stringent regulations govern the manufacturing and supply of biologics products, thus impacting the production and release schedules of such products more significantly.

Failure or delay in development of new product candidates that achieve commercial success could adversely frustrate the achievement of development targets, adversely affect the reputation of the Issuer's R&D capabilities, and is likely to materially adversely affect its business and results of operations.

Since the Issuer's business model and strategy relies on the success of relatively few compounds, the failure of any compound in its late-stage pipeline or in-line products may have a significant negative effect on its business or results of operations.

Significant delays to anticipated launch dates of new products could have a material adverse effect on the Issuer's financial condition and/or results of operations. For example, for the launch of products that are seasonal in nature, delays in regulatory approvals or manufacturing difficulties may delay launch to the next season which, in turn, may significantly reduce the return on costs incurred in preparing for the launch for that

season. Furthermore, in immuno-oncology for example, speed to market is critical given the large number of clinical trials being conducted by other companies.

In addition, a delayed launch may lead to increased costs if, for example, marketing and sales efforts need to be rescheduled or performed for longer than expected.

In addition to developing products in-house, the Issuer seeks technology licensing arrangements and strategic collaborations to expand its product portfolio and geographical presence as part of its business strategy. Such licensing arrangements and strategic collaborations are key, enabling the Issuer to grow and strengthen the business. The success of such arrangements is largely dependent on the technology and other intellectual property ("IP") rights the Issuer acquires or licenses, and the resources, efforts and skills of its partners. Disputes or difficulties in the Issuer's relationship with its collaborators or partners may arise, for example, due to conflicting priorities or conflicts of interest between parties.

Also in many cases, the Issuer makes milestone payments well in advance of the commercialisation of the products, with no assurance that it will recoup these payments.

The Issuer experiences strong competition from other pharmaceutical companies in respect of licensing arrangements, strategic collaborations, and acquisition targets.

Failure to complete collaborative projects in a timely, cost-effective manner may limit the Issuer's ability to access a greater portfolio of products, IP technology and shared expertise. Disputes and difficulties with the Issuer's partners may erode or eliminate the benefits of its alliances and collaborations. In addition, failure to perform on the part of parties to externalisation transactions may diminish the future value of those transactions or, in some cases, allow a competitor to beat the Issuer to market with a similar or first-in-class product. Delay of launch can also erode the term of patent exclusivity.

Competition from other pharmaceutical companies means that the Issuer may be unsuccessful in implementing some of its intended projects or it may have to pay a significant premium over book or market values for its acquisitions.

Difficulties in obtaining or maintaining regulatory drug approval for products

The Issuer is subject to strict controls on the commercialisation processes for its pharmaceutical products, including their development, manufacture, distribution and marketing. The criteria for establishing safety, efficacy and quality, which are essential for securing marketing approvals, vary by country and by region. Regulators can refuse to grant approval or may require additional data before approval is granted or as a post-approval commitment, even though the medicine may already be approved or launched in other countries.

Factors, including advances in science and technology, evolving regulatory science, new laws and policies, and different approaches to benefit/risk tolerance by regulatory authorities, the general public, and other third-party public interest groups are known to influence the approvability of new drugs. While the Issuer seeks to manage most of these risks, unanticipated and unpredictable policymaking by governments and regulators, limited regulatory authority resources or conflicting priorities often lead to delays in regulatory approvals.

The Issuer may be required to generate additional data after a drug is approved because a regulatory authority may have concerns that impact the benefit/risk profile of the drug. For the Issuer's marketed drugs, new data or meta-analyses have the potential to drive changes in the approval status or labelling. In addition, recent years have seen an increase in post-marketing regulatory requirements and commitments, an increased call for third-party access to regulatory and clinical trial data packages for independent analysis and interpretation, and broader data transparency. Such transparency, while important, could lead to inappropriate or incorrect data analyses which may damage the integrity of the Issuer's products and its reputation.

Delays in regulatory reviews and approvals could delay the Issuer's ability to market its products and may adversely affect its revenue. In addition, post-approval requirements, including additional clinical trials, could result in increased costs, and may impact the labelling and approval status of currently marketed products.

With the United Kingdom (the "UK") potentially leaving the European Union (the "EU") ("**Brexit**") by the end of October 2019 (see "*Risk Factors - Uncertainty and volatility in relation to the UK's planned exit from the EU*"), intense work is ongoing to manage Brexit related changes, identify scenarios for the many uncertainties still to be resolved, and determine the new UK requirements moving forward. This includes transferring licences and authorisations for EU markets currently held in the UK to an EU member state and

building capability to test medicines in the EU for which such testing is currently undertaken in the UK. UK licences also need to be separated out from centrally approved products in the EU. These actions are required to ensure appropriate regulatory requirements can be met both in the EU and UK post October 2019. Based on the Issuer's corporate planning assumptions for a no deal Brexit, with no transition period, the Issuer is taking steps to protect product supply both in the UK and EU. Changes in regulatory reviews and approvals, and safety surveillance will certainly have implications on resources, ways of working and costs.

Failure to obtain, defend and enforce effective IP protection and IP challenges by third-parties

A pharmaceutical product may be protected from being copied for a limited period of time under certain patent rights and/or related IP rights, such as regulatory data protection or orphan drug status. Typically, products protected by such rights generate significantly higher revenues than those not protected. The Issuer's ability to obtain, maintain, defend and enforce patents and other IP rights in relation to its products is an important element in of its ability to protect and recoup its investment in R&D and create long-term value for the business. Some countries in which the Issuer operates do not offer robust IP protection. This may be because IP laws are still developing, the scope of those laws is limited or the political environment does not support such legislation. The Issuer also recognises increasing use of compulsory licensing in some of the countries in which it operates.

The Issuer may also face challenges early in the patent application process and throughout a patent's life. The grounds for these challenges could be the validity of a patent and/or its effective scope and are based on ever-evolving legal precedents. The Issuer is experiencing increased challenges in the United States of America (the "US") and elsewhere in the world and there can be no guarantee of success for either party in patent proceedings and litigation.

The Issuer also bears the risk that its products may be found to infringe patents owned or licensed by third-parties, including research-based and generic pharmaceutical companies and individuals. These third-parties may seek remedies for patent infringement, including injunctions (for example, preventing the marketing of one of the Issuer's products) and damages (for example, research-based competitors are alleging infringement of their patents and are seeking damages in relation to the Issuer's marketing of *Imfinzi* and *Calquence*).

Limitations on the availability of patent protection, the ability to obtain related IP rights or the use of compulsory licensing in certain countries in which the Issuer operates, as well as its ability to defend and enforce its patents, could allow for earlier entry of generic or biosimilar competitor products. This could have a material adverse effect on the pricing and sales of its products and, consequently, could materially adversely affect its revenues.

Third-parties may be awarded remedies for alleged infringement of their IP, for example injunctions and damages for alleged patent infringement. In the US, courts may order enhanced (up to treble) damages for alleged wilful infringement of patents. From time to time the Issuer may acquire licences, discontinue activities and/or modify processes to avoid claims of patent infringement. These steps could entail significant costs and the Issuer's revenue and margins could be materially adversely affected.

Commercialisation Risks

Competitive pressures including expiry or loss of IP rights and generic competition

The Issuer's pharmaceutical products compete with other products marketed by research-based pharmaceutical companies and with generic or biosimilar drugs marketed by generic drug manufacturers.

Generic versions of products, including biosimilars, are often sold at lower prices than branded products, as the manufacturer does not have to recoup the significant cost of R&D investment and market development. Expiry or loss of IP rights can materially adversely affect the Issuer's revenues and financial condition due to the launch of cheaper generic copies of the product in the country where the rights have expired or been lost. For example in 2018, the Issuer's US product sales of *Crestor* fell to US\$170 million (2017: US\$373 million), following the launch of generics.

Additionally, the expiry or loss of patents covering other innovator companies' products may also lead to increased competition and pricing pressure for the Issuer's own, still-patented products in the same product class due to the availability of generic products in that product class.

Generic manufacturers may also take advantage of the failure of certain countries to properly enforce regulatory data protection or other related IP rights and may launch generics during this protected period. This is a

particular risk in some emerging markets where appropriate patent protection or other related IP rights may be difficult to obtain or enforce.

The biosimilars market experienced notable growth since 2017, with approval of several monoclonal antibody biosimilars in the US and Europe. Management expects this trend to continue. Increased regulatory and legal activity related to the launch and approval of these therapeutics is anticipated. Regulatory authorities in other territories continue to implement or consider abbreviated approval processes for biosimilars, allowing quicker entry to market for such products and earlier than anticipated competition for patented biologics.

As well as facing generic competition upon expiry or loss of IP rights, the Issuer also faces the risk that generic drug manufacturers seek to market generic versions of its products prior to expiries of its patents and/or the Regulatory Exclusivity periods. For example, the Issuer is currently facing challenges from numerous generic drug manufacturers regarding its patents relating to key products, including *Symbicort*, *Brilinta*, *Faslodex* and *Farxiga*.

IP rights protecting the Issuer's products may be challenged by external parties. The Issuer expects its most valuable products to receive the greater number of challenges. Despite the Issuer's efforts to establish and defend robust patent protection for its products, it bears the risk that courts may decide that its IP rights are invalid and/or that third-parties do not infringe its asserted IP rights.

Where the Issuer asserts its IP rights but is ultimately unsuccessful, third-parties may seek damages, alleging, for example, that they have been inappropriately restrained from entering the market. In such cases, the Issuer bears the risk that it incurs liabilities to those third-parties.

If the Issuer is not successful in obtaining, maintaining, defending or enforcing its exclusive rights to market its products, particularly in the US where it achieves its highest product sales, its revenue and margins could be materially adversely affected. In addition, unsuccessful assertion of the Issuer's IP rights may lead to damages or other liabilities to third-parties that could materially adversely affect the Issuer's financial performance.

Approval of competitive products for the same or similar indication as one of the Issuer's products may result in immediate and significant decreases in the Issuer's revenues.

Unfavourable resolution of current and potential future patent litigation may require the Issuer to make significant provisions in its accounts relating to legal proceedings and/or could materially adversely affect its financial condition or results of operations.

Price controls and reductions

Most of the Issuer's key markets have experienced the implementation of various cost control or reimbursement mechanisms in respect of pharmaceutical products.

In the US, there is significant pricing pressure driven by payer consolidation, restrictive reimbursement policies, and cost control tools, such as exclusionary formularies and price protection clauses. Many formularies employ 'generic first' strategies and/or require physicians to obtain prior approval for the use of a branded medicine where a generic alternative exists. These mechanisms can be used by payers to limit the use of branded products and put pressure on manufacturers to reduce net prices. In addition, patients are seeing changes in the design of their health plan benefits and may experience variation in how their plans cover their medications, including increases in the out-of-pocket payments for their branded medications. Patient out-of-pocket spending is generally in the form of a co-payment or co-insurance, but there is a growing trend towards high deductible health plans that require that patients pay the full list price of their drugs and services until they meet certain out-of-pocket thresholds.

The US political landscape continues to consider a range of legislative and regulatory proposals to address the high costs of prescription drugs as well as reforms to the US healthcare system. The Issuer faces uncertainty due to federal legislative and administrative efforts to repeal, substantially modify or invalidate some or all of the provisions of the Affordable Care Act (the "ACA"). Additionally, there may be modifications to Medicare and other government programmes, price transparency requirements and policies aimed at reducing drug list prices. It is difficult to predict what specific proposals could be enacted and to determine the implications for the healthcare system and pharmaceutical industry. However, lowering drug costs remains a key campaign promise of the current administration and proposals that would significantly modify existing laws and regulations, including coverage and reimbursement of drugs in government programmes and policies relating

to drug pricing, could affect private health insurance, coverage and reimbursement in Medicare, Medicaid and the health insurance exchange marketplaces, and other facets of the US healthcare market, with potentially significant impacts on the pharmaceutical industry.

Any future replacement, modification or repeal of the ACA, or any significant spending reductions or cost controls affecting Medicare, Medicaid or other publicly funded or subsidised health programmes in the US, could adversely affect the Issuer's business and financial results. The significant uncertainty about the future of the ACA, entitlement reform and healthcare laws in general in the US could have a material adverse effect on the Issuer's results of operations, financial condition or business.

Ongoing scrutiny of the US pharmaceutical industry, focused largely on pricing, is placing increased emphasis on the value of medications. This scrutiny will likely continue across many stakeholders, including policymakers and legislators.

In the US, consolidation among distributors, retail pharmacy chains and other purchasing organisations, including integration across the supply chain, creates concentration of credit risk and increasing potential for large integrated entities to exert more power in negotiations with the Issuer and its subsidiaries (the "**Group**"), which could result in margin erosion.

The Issuer expects that consolidation and integration of drug distributors, retail pharmacy chains, private insurers, managed care organisations and other purchasing organisations may continue to have an effect on pharmaceutical manufacturers, including the Issuer.

In Europe, the pharmaceutical industry continues to be exposed to various ad hoc cost-containment measures and reference pricing mechanisms, which impact prices. There is a trend towards increasing transparency and comparison of prices among EU Member States which may eventually lead to a change in the overall pricing and reimbursement landscape. There is also a continued push across the EU to harmonise the Health Technology Assessment ("**HTA**") review process. This could lead to an environment in the EU where medicines undergo duplicate HTA evaluations, both at an EU level and a country level, as the Issuer believes it is unlikely organisations such as GBA Pharma in Germany or Haute Autorité de Santé in France would make changes to their systems.

The potential duplication of HTA evaluations could result in a delay to times of reimbursement and patient access.

In emerging markets, governments are increasingly controlling pricing in the self-pay sector and favouring locally manufactured drugs. In addition, the emergence of price referencing has been seen in some markets combined with a call from authorities to provide greater global price transparency.

Concurrently, many markets are adopting the use of HTA to provide a rigorous evaluation of the clinical efficacy of a product at, or post, launch. HTA evaluations are also increasingly being used to assess the clinical effect, as well as cost-effectiveness, of products in a particular health system. This comes as payers and policymakers attempt to drive increased efficiencies in the use and choice of pharmaceutical products.

Due to these pressures on the pricing of the Issuer's products, there will continue to be downward pressure on prices globally that will challenge the profitability levels of products in particular markets.

The continued disparities in EU and US pricing systems could lead to marked price differentials between regions, which, by way of the implementation of existing or new reference pricing mechanisms, increases the pricing pressure affecting the industry. The importation of pharmaceutical products from countries where prices are low due to government price controls, or other market dynamics, to countries where prices for those products are higher, is already prevalent and may increase. Strengthened collaboration by governments may accelerate the development of further cost-containment policies (such as joint procurement). Increased and simplified access to national and regional prices in markets and the publication of these prices in centralised databases have facilitated the uptake and efficiency of price referencing across the world.

Economic, regulatory and political pressures

The Issuer operates in over 100 countries and is subject to political, socio-economic and financial factors (including foreign exchange movements) both globally and in individual countries.

A sustained global economic downturn may further exacerbate pressure from governments and other healthcare payers on medicine prices and volumes of sales in response to pressures on budgets, and may cause a slowdown or a decline in growth in some markets. Those governments most severely impacted by the economic downturn may seek alternative ways to settle their debts through, for example, the issuance of government bonds which might trade at a discount to the face value of the debt. The Issuer's customers may cease to trade, which may result in losses from writing off debts, or a reduction in demand for the Issuer's products.

Deterioration of, or failure to improve, socio-economic conditions, and situations and/or resulting events, depending on their severity, could adversely affect the Issuer's supply and/or distribution chain in the affected countries and the ability of customers or ultimate payers to purchase its medicines. This could adversely affect the Issuer's business or results of operations.

The Issuer is highly dependent on being able to access a sustainable flow of liquid funds due to the high fixed costs of operating its business and the long and uncertain development cycles of its products. In a sustained economic downturn, financial institutions with whom it deals may cease to trade and there can be no guarantee that it will be able to access monies owed to it without a protracted, expensive and uncertain process, if at all.

The majority of the Issuer's cash investments are managed centrally and are invested in collateralised bank deposits, fixed income securities in government, financial and non-financial securities, and AAA credit-rated institutional money market funds. Money market funds are backed by institutions in the US, EU or elsewhere, which, in turn, invest in other funds, including sovereign funds. This means the Issuer's credit exposure is a mix of US, EU and rest of the world sovereign default risk, financial institution and non-financial institution default risk.

A number of the Issuer's existing or future commercial or other agreements, such as borrowings, derivative financial instruments and commercial contracts, utilise or may utilise LIBOR or other similar rates as benchmark reference rates. LIBOR and other benchmark reference rates are the subject of ongoing national and international regulatory reform, the result of which could see them partially or fully replaced by alternative reference rates, with potential adjustments or renegotiations being necessary to the Issuer's agreements in respect of the commercial terms or mechanisms to set the reference rate. Whilst different alternative reference rates could develop for different currencies and for different agreements, for example borrowings and derivative financial instruments, there is a risk that that Issuer fails to renegotiate its agreements. Any combination of these events could have an adverse effect on the cost, cash flows, value, return on and trading market of (as appropriate) the Issuer's borrowings, derivative financial instruments, commercial and other agreements, and could increase the Issuer's administrative burden if the transition to alternative rates is required or necessary by regulation or market practice. (See also "*Risk Factors - There are risks that certain benchmark rates may be administered differently or discontinued in the future, including the potential phasing-out of LIBOR after 2021, which may adversely affect the trading market for, value of and return on, Notes based on such benchmarks*".)

While the Issuer has adopted cash management and treasury policies to manage the risk of not being able to access a sustainable flow of liquid funds, it cannot be certain that these will be as effective as they are intended to be, in particular in the event of a global liquidity crisis. In addition, open positions where the Issuer is owed money and investments that the Issuer has made in financial and non-financial institutions or money market funds cannot be guaranteed to be recoverable. Additionally, if the Issuer needs access to external sources of financing to sustain and/or grow its business, such as the debt or equity capital financial markets, this may not be available on commercially acceptable terms, if at all, in the event of a severe and/or sustained economic downturn. This may, for instance, be the case in the event of any default by the Issuer on its debt obligations, which may materially adversely affect the Issuer's ability to secure debt funding in the future or its financial condition in general.

Uncertainty and volatility in relation to the UK's planned exit from the EU

On 23 June 2016, the UK held a referendum on the UK's continuing membership of the EU, the outcome of which was a decision for the UK to leave the EU. On 29 March 2017, the UK Government formally notified the EU under Article 50 of the UK's intention to leave the EU. This notification began the process of negotiation that will likely determine the future terms of the UK's relationship with the EU. Absent a negotiated agreement, the UK will leave the EU on 31 October 2019 and relevant EU law and agreements will cease to apply.

It is still too early to judge the full impact of Brexit. While a draft Withdrawal Agreement has been agreed between the UK government and the European Commission, it is unclear whether this will be ratified by the

UK parliament in its current form, amended, or if the UK will leave the EU without a deal. In the event that a withdrawal agreement is ratified by the UK parliament, the UK may leave the EU before 31 October 2019. Existing arrangements would be maintained for a transition period while the future relationships between the UK and the EU were negotiated. In the absence of a ratified agreement, it is unclear what trading relationships the UK will have with the EU and other significant trading partners after 31 October 2019 given the range of political and legal options currently available including, for example, a no deal exit from the EU, extension or rescission of the Article 50 notice and a second referendum. Brexit and the implementation of the resulting changes could materially and adversely affect the tax, tax treaty, currency, operational, legal and regulatory regimes as well as the macro-economic environment in which the Group operates. Since the referendum, global markets and foreign exchange rates have experienced increased volatility, including a decline in the value of pound sterling as compared to the euro and US dollar. Upon leaving the EU, among other things, the UK could lose access to the single EU market, travel between the UK and EU countries could be restricted and border checks or other regulatory constraints may impede the free movement of goods. The Issuer's workforce, and in turn its ability to recruit and retain talent, could be impacted by any restrictions on the movement of persons as 3.9 per cent. of the Issuer's employees in the UK are citizens of EU countries other than the UK. The Issuer could face new and greater costs and challenges if UK regulations and policies that govern its business diverge from those of the EU, or if there is any other new or increased friction in the Issuer's trading environment.

Until the Brexit negotiation process is completed, it is difficult for the Issuer to anticipate the potential impact on its market share, sales, profitability and results of operations. For example, it is possible in the immediate aftermath of the UK leaving the EU that the capacity at major ports both in the UK and the EU is materially reduced for an indeterminate period of time. This could adversely affect the Issuer's ability to transport medicines and raw materials/intermediates to the EU and *vice versa* with a consequential adverse impact.

The longer-term effects of Brexit are difficult to predict but could include further financial instability and slower economic growth or economic downturn in the UK in particular, but also in Europe and the global economy. Any restrictions on the movement of persons, deterioration in market access or trading terms, delay or restrictions to the movement of goods or increased cost and burdens in the form of new or diverging rules and regulations may have a significant adverse impact on the Issuer's operations, profitability and business model. Further, uncertainty around the form and timing of any withdrawal agreement and the form and timing of any post-withdrawal trading arrangements (whether with the EU or third parties) could increase volatility and lead to adverse effects on the economy of the UK, other parts of Europe and the rest of the world, which in turn could have an adverse economic impact on the Issuer's operations.

Failure or delays in the quality and execution of commercial strategies

The commercial success of the Issuer's products and markets, including the development of growth markets, is a critical factor in sustaining or increasing global product sales and replacing lost product sales due to patent expiry. The successful launch of a new pharmaceutical product involves substantial investment in sales and marketing activities, launch stocks and other items. The Issuer may ultimately be unable to achieve commercial success for various reasons, including difficulties in manufacturing sufficient quantities of the product candidate for development or commercialisation in a timely manner, the impact of price control measures imposed by governments and healthcare authorities, the outcome of negotiations with third-party payers, erosion of IP rights, including infringement by third-parties, failure to show a differentiated product profile and changes in prescribing habits.

Failure to execute the Issuer's commercial strategies could materially adversely impact its business or results of operations.

If a new product does not succeed as anticipated or its rate of sales growth is slower than anticipated, there is a risk that the Issuer may be unable to fully recoup the costs incurred in launching it, which could materially adversely affect its business or results of operations.

The commercialisation of biologics is often more complex than for small molecule pharmaceutical products, primarily due to differences in the mode of administration, technical aspects of the product, and rapidly changing distribution and reimbursement environments. These factors could materially adversely impact the Issuer's revenues from the sales of biologic medicines, such as *Synagis* and *FluMist/Fluenz*.

The Issuer faces particular challenges in emerging markets, including: (i) more volatile economic conditions and/or political environments; (ii) competition from multinational and local companies with existing market presence; (iii) difficulties enforcing and protecting IP; (iv) inadequate protection against crime (including

counterfeiting, corruption and fraud); (v) the need to impose developed market compliance standards; (vi) the need to meet a more diverse range of national regulatory, clinical, manufacturing and distribution requirements; (vii) potential inadvertent breaches of local and international law and the need to manage sanctions and other restrictions that may be imposed in each jurisdiction; (viii) recruitment of appropriately skilled and experienced personnel; (ix) difficulty in identifying the most effective sales and marketing channels and routes to market; (x) intervention by local or national governments or regulators restricting market access and/or introducing adverse price controls; (xi) difficulty in managing local partnerships such as co-promotion and co-marketing; in terms of performance and adherence to the Issuer's compliance standards which are often higher than the market standard; (xii) difficulties in cash repatriation due to strict foreign currency controls, risk of material currency devaluation and lack of hard currency reserves in some emerging markets; and (xiii) complexity derived from direct exports to countries where the Issuer does not have a legal entity.

The failure to exploit potential opportunities appropriately in emerging markets or materialisation of the risks and challenges of doing business in such markets, including inadequate protection against crime (including counterfeiting, corruption and fraud) or inadvertent breaches of local and international law may materially adversely affect the Issuer's reputation, business or results of operations.

The Issuer may also seek to acquire complementary businesses or enter into other strategic transactions. The integration of an acquired business could involve incurring significant debt and unknown or contingent liabilities, as well as having a negative effect on its reported results of operations from acquisition-related charges, amortisation of expenses related to intangibles and charges for the implementation of long-term assets. The integration of new businesses with the Issuer's business could result in operational complexities.

The Issuer may also experience difficulties in integrating geographically separated organisations, systems and facilities, and personnel with different organisational cultures. Disputes or difficulties in the Issuer's relationship with its collaborators or partners may also arise, often due to conflicting priorities or conflicts of interest between parties.

Integration processes relating to strategic transactions may also result in business disruption, diversion of management resources, the loss of key employees and other issues, such as a failure to integrate information technology ("IT") and other systems.

Incurrence of significant debt or liabilities due to the integration of an acquired business could cause deterioration in the Issuer's credit rating and result in increased borrowing costs and interest expense.

Supply Chain and Business Execution Risks

Failure to maintain supply of compliant, quality products

The Issuer may experience difficulties, delays and interruptions in the manufacturing and supply of its products for various reasons, including: (i) demand significantly in excess of forecast demand, which may lead to supply shortages (which is particularly challenging before product launch); (ii) supply chain disruptions, including those due to natural or man-made disasters at one of its facilities, at a critical supplier or vendor, or during transit; (iii) delays in construction of new facilities or the expansion of existing facilities, including those intended to support future demand for its products (particularly as the complexities associated with biological facilities, especially for drug substances, increase the probability of delay); (iv) the inability to supply products due to a product quality failure or regulatory compliance action such as licence withdrawal, product recall or product seizure; and (v) other manufacturing or distribution problems, including changes in manufacturing production sites, limits to manufacturing capacity due to regulatory requirements, changes in the types of products produced, or physical limitations or other business interruptions that could impact continuous and adequate supply.

As with the rest of the pharmaceutical industry, the Issuer works in a heavily regulated environment. It is necessary for the Issuer to meet all regulations, including compliance with Good Manufacturing Practices and Good Distribution Practices and comparable regulatory dossier conditions of approval in other countries in which its products are licensed, manufactured or sold. Regulatory agencies periodically inspect the Issuer's manufacturing facilities to evaluate compliance with applicable requirements and may identify potential deficiencies.

The Issuer increasingly relies on third-parties for the timely supply of goods, such as raw materials (for example, the active pharmaceutical ingredient in some of its medicines and drug substances and/or finished drug products

for some of its biologic medicines), equipment, formulated drugs and packaging, critical product components and services, all of which are key to its operations. Many of these goods are difficult to substitute in a timely manner or at all. The Issuer expects that external capacity for biologics drug substance production will remain constrained for the next few years and, accordingly, may not be readily available for supplementary production in the event that it experiences an unforeseen need for such capacity.

Difficulties with manufacturing and supply, forecasting, distribution or third-party suppliers may result in product shortages, which may lead to lost product sales and materially adversely affect the Issuer's reputation and revenues. Even slight variations in components or any part of the manufacturing process may lead to a product that is non-compliant and does not meet quality standards. This could lead to recalls, spoilage, product shortage, regulatory action and/or reputational harm.

Failure to comply with all manufacturing regulations can result in negative regulatory inspection findings leading to manufacturing cessation, product seizure, debarment or recalls which could have a material adverse effect on the Issuer's business, financial condition and results of operations.

Illegal trade in the Issuer's products

The illegal trade in pharmaceutical products is widely recognised by the pharmaceutical industry, non-governmental organisations and governmental authorities to be increasing. Illegal trade includes counterfeiting, theft and illegal diversion (that is, when the Issuer's products are found in a market where it did not send them and where they are not approved or not permitted or allowed to be sold). There is a risk to public health when illegally traded products enter the supply chain, as well as associated financial risk. Authorities and the public expect the Issuer to help reduce opportunities for illegal trade in the Issuer's products through securing its supply chains, surveillance, investigation and supporting legal action against those found to be engaged in illegal trade.

Public loss of confidence in the integrity of pharmaceutical products as a result of illegal trade could materially adversely affect the Issuer's reputation and financial performance. In addition, undue or misplaced concern about this issue may cause some patients to stop taking their medicines, with consequential risks to their health. Authorities may take action, financial or otherwise, if they believe the Issuer is liable for breaches in its own supply chains.

There is also a direct financial loss when, for example, counterfeit and/or illegally diverted products replace sales of genuine products in a market or genuine products are recalled following discovery of counterfeit products.

Reliance on third-party goods and services

The Issuer spends approximately US\$10 billion each year with trade suppliers. This expenditure supports the length of the Issuer's value chain from discovery to manufacture and commercialisation of its medicines.

Many of the Issuer's business-critical operations, including certain R&D processes, IT systems, human resources, finance, tax and accounting services have been outsourced to third-party providers. The Issuer is therefore heavily reliant on these third-parties not just to deliver timely and high quality services, but also to comply with applicable laws and regulations and adhere to its ethical business expectations of third-party providers.

The failure of outsource providers to deliver timely services, and to the required level of quality, or the failure of outsource providers to co-operate with each other, could materially adversely affect the Issuer's financial condition or results of operations. Moreover, the failure of these third-parties to operate in an ethical manner could adversely impact the Issuer's reputation, both internally and externally, or even result in non-compliance with applicable laws and regulations.

The Issuer's business and financial results could also be materially adversely affected by disruptions caused by its failure to successfully manage either the integration of outsourced services or the transition process of insourcing services from third-parties.

Failure of information security, data protection and cybercrime

The Issuer is dependent on effective IT systems. These systems support key business functions such as its R&D, manufacturing, supply chain and sales capabilities. They provide an important means of safeguarding and

communicating data, including critical or sensitive information, the confidentiality and integrity of which the Issuer relies on. The Issuer also relies on the effectiveness of its internal policies, controls and procedures to protect the confidentiality, integrity and availability of information held on its IT systems, as well as the effectiveness of its due diligence of, and ongoing oversight over, third-party vendors who have access to the Issuer's data. In addition, the Issuer must ensure that the personal data which it, or third-party vendors operating on its behalf, holds and processes is protected in a manner that complies with the EU Directive 95/46/EC (General Data Protection Regulation) ("GDPR") which entered into force in May 2018.

Examples of sensitive information that the Issuer protects include clinical trial records (patient names and treatments), personal information (employee bank details, home address), IP related to manufacturing process and compliance, key research science techniques, the Issuer's property (i.e. from theft) and privileged access (rights to perform IT tasks).

The size and complexity of the Issuer's IT systems and cloud utilisation, and those of its third-party vendors (including outsource and "Software as a Service" providers) with whom it contracts, have significantly increased over the past decade. Such systems are potentially vulnerable to service interruptions and security breaches from attacks by malicious third-parties, or from intentional or inadvertent actions by its employees or vendors.

Significant changes in the business footprint and the implementation of the IT strategy, including the creation and use of captive offshore global technology centres, could lead to temporary loss of capability.

Any significant disruption to these IT systems (including breaches of data security or cybersecurity, failure to integrate new and existing IT systems) or failure to comply with additional requirements under the GDPR and other applicable laws, could harm the Issuer's reputation and materially adversely affect its financial condition or results of operations.

While the Issuer invests heavily in the protection of its data and IT, it may be unable to prevent breakdowns or breaches in its systems or failures of its cybersecurity policies, controls or procedures. Any such breakdown, breach or failure could result in disclosure of confidential or other sensitive information, damage to its reputation, regulatory penalties, or sanctions, financial losses and/or other costs.

The inability to effectively back up and restore data could lead to permanent loss of data that could in turn result in non-compliance with applicable laws and regulations, and otherwise harm the Issuer's business.

The Issuer and its vendors could be susceptible to third-party or internal attacks on their information security systems. Such attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including organised criminal groups, 'hacktivists', nation states, employees, and others. From time to time the Issuer experiences intrusions, including as a result of computer-related malware. The Issuer may be unable to ward off such attacks which could have an adverse effect on its business.

Although the Issuer maintains cybersecurity insurance, there can be no assurance that its insurance coverage limits will protect against any future claim or that such insurance proceeds will be paid to the Issuer in a timely manner.

The Issuer increasingly uses the internet, digital content, social media, mobile applications, the internet of things, and other forms of new technology to communicate internally and externally. The accessibility and instantaneous nature of interactions with such media may facilitate or exacerbate the risk of unauthorised data loss from within the Issuer. It may also lead to false or misleading statements being made about the Issuer, which may damage its reputation, brand image or goodwill. As existing social media platforms expand and evolve, and new social media platforms emerge, it becomes increasingly challenging to identify new points of entry and to put structures in place to secure and protect sensitive information.

The GDPR and similar privacy legislation being passed in various jurisdictions globally introduce the obligation to report data protection breaches, whether intentional or inadvertent, to regulators and affected individuals within expedited timeframes. Such expedited reporting, often before the nature and impact of a data breach can be fully understood, could potentially cause reputational damage and a loss of public trust that ultimately may be disproportionate to the extent of the breach.

Inappropriate use of certain media vehicles could lead to the unauthorised or unintentional public disclosure of sensitive information (such as personally identifiable information on employees, healthcare professionals or patients, such as those enrolled in the Issuer's clinical trials), which may damage the Issuer's reputation, adversely affect its business or results of operations and expose it to legal risks and/or additional legal obligations. Similarly, the involuntary public disclosure of commercially sensitive information or an information loss could adversely affect the Issuer's business or results of operations. In addition, negative posts or comments about the Issuer (or, for example, the safety of any of the Issuer's products) on social media websites or other digital channels could harm the Issuer's reputation, brand image or goodwill.

Failure of critical processes

Unexpected events and/or events beyond the Issuer's control could result in the failure of critical processes within the Issuer or at third-parties on whom the Issuer is reliant. The Issuer's business faces threats to business continuity from many directions. Examples of material threats include: (i) disruption to the Issuer's business or the global markets if there is instability in a particular geographic region, including as a result of war, terrorism, pandemics, armed conflicts, riots, unstable governments, civil insurrection or social unrest; (ii) natural disasters in areas of the world prone to extreme weather events and earthquakes; and (iii) cyber threats similar to those detailed in the "*Failure of information security, data protection and cybercrime*" section above.

Failure of critical processes may result in an inability to research, manufacture or supply products to patients. The Issuer has developed a Business Resilience framework which is designed to mitigate such risks. However, there is no guarantee that these measures will be sufficient to prevent business interruption.

This may expose the Issuer to litigation and/or regulatory action which may result in fines, loss of revenue and adversely affect the Issuer's financial results.

Any expected gains from productivity initiatives are uncertain

The Issuer continues to implement various productivity initiatives and restructuring programmes with the aim of enhancing the long-term efficiency of the business. However, anticipated cost savings and other benefits from these programmes are based on estimates and the actual savings may vary significantly or may not be achieved at all. In particular, these cost-reduction measures are often based on current conditions and cannot always take into account any future changes to the pharmaceutical industry or the Issuer's operations, including new business developments or wage or price increases.

The Issuer's failure to successfully implement these planned cost-reduction measures, either through the successful implementation of employee relations processes (including consultation, engagement, talent management, recruitment and retention), or the possibility that these efforts do not generate the level of cost savings it anticipates, could materially adversely affect its business or results of operations.

Failure to attract and retain key personnel, and engage successfully with its employees

The Issuer relies heavily on recruiting and retaining talented employees with a diverse range of skills and capabilities to meet its strategic objectives.

The Issuer faces intense competition for qualified individuals, as the supply of people with specific skills and significant leadership potential or in specific geographic regions may be limited and in the UK the added uncertainty created by Brexit could impact the hiring and retention of staff in some business-critical areas.

The inability to attract and/or retain highly-skilled personnel may weaken the Issuer's succession plans for critical positions in the medium term, may materially adversely affect the implementation of the Issuer's strategic objectives and could ultimately impact the Issuer's business or results of operations.

The successful delivery of the Issuer's business objectives is dependent on high levels of engagement, commitment and motivation of the workforce. In January 2019, the Issuer announced organisational changes to support continued scientific innovation and commercial success relating to the next phase in its strategic development. Such changes may increase levels of employee uncertainty leading to lower levels of engagement.

Failure to engage effectively with its employees could lead to business disruption in the Issuer's day-to-day operations, reduce levels of productivity and/or increase levels of voluntary turnover, all of which could ultimately materially adversely affect the Issuer's business or results of operations.

Legal, Regulatory and Compliance Risks

Failure to adhere to applicable laws, rules and regulations

The Issuer's business operations are subject to a wide range of laws, rules and regulations from governmental and non-governmental bodies around the world.

Any failure to comply with these applicable laws, rules and regulations may result in the Issuer being investigated by relevant agencies and authorities and/or in legal proceedings being filed against the Issuer. Such investigations or proceedings could result in the Issuer becoming subject to civil and/or criminal sanctions and/or being forced to pay fines or damages. Relevant authorities have wide-ranging administrative powers to deal with any failure to comply with continuing regulatory oversight and this could affect the Issuer, whether such failure is the Issuer's own or that of its contractors or external partners. Moreover, such laws, rules and regulations are subject to change.

Material examples of statutes, rules and regulations impacting business operations include: (i) compliance with Good Manufacturing Practice; (ii) local, national and international environmental and occupational health and safety laws; (iii) trade control laws governing the Issuer's imports and exports including nationally and internationally recognised trade agreements, embargoes, trade and economic sanctions and anti-boycott requirements; (iv) competition laws and regulations, including challenges from competition authorities and private damages actions; (v) rules and regulations established to promote ethical supply chain management; (vi) financial regulations including, but not limited to, external financial reporting, taxation and money laundering; (vii) employment practices; (viii) disclosure of payments to healthcare professionals under The Physician Payments Sunshine Act and European Federation of Pharmaceutical Industries and Associations legislation; (ix) appropriate disclosure of community support, patient group support and product donations; and (x) compliance with human rights and appropriate environmental practices of third-party contractors around the world including with, but not limited to, the conflict minerals rule in the US, and the UK Modern Slavery Act.

The Issuer has environmental and/or occupational health and safety-related liabilities at some current, formerly owned, leased and third-party sites. The Issuer's failure to comply with applicable laws, rules and regulations; manage its liabilities; or to adequately anticipate or proactively manage emerging policy and legal developments could materially adversely affect its licence to operate, or results of operations; adversely affect its reputation; cause harm to people or the environment; and/or lead to fines or other penalties. For example, once a product has been approved for marketing by the regulatory authorities, it is subject to continuing control and regulation, such as the manner of its manufacture, distribution, marketing and safety surveillance. If regulatory issues concerning compliance with environmental, current Good Manufacturing Practice or Safety monitoring regulations for pharmaceutical products (often referred to as pharmacovigilance) arise, this could lead to product recalls, loss of product approvals, and seizures, and interruption of production, which could create product shortages and delays in new product approvals, and negatively impact patient access. As another example, violation of laws, rules, regulations or policies in countries subject to trade and economic sanctions could lead to loss of import or export privileges, civil or criminal penalties for the Issuer or its employees, or potential reputational harm, which could have a material adverse effect on the Issuer's results of operations, financial condition or business.

Safety and efficacy of marketed products may be questioned

The Issuer's ability to accurately assess, prior to launch, the eventual safety or efficacy of a new product once in broader clinical use can only be based on data available at that time, which is inherently limited due to relatively short periods of product testing and relatively small clinical study patient samples.

Any unforeseen safety concerns or adverse events relating to its products or failure to comply with laws, rules and regulations relating to provision of appropriate warnings concerning the dangers and risks of its products that result in injuries could expose the Issuer to large product liability damages claims, settlements and awards, particularly in the US. Such claims could be costly, divert management attention or damage the Issuer's reputation and demand for its products.

Adverse publicity relating to the safety of a product or of other competing products may increase the risk of product liability claims. Serious safety concerns or adverse events relating to the Issuer's products could lead to product recalls, seizures, loss of product approvals, declining sales and interruption of supply and could materially adversely impact patient access, the Issuer's reputation and financial revenues.

Unfavourable resolution of such current and similar future product liability claims could subject the Issuer to enhanced damages, consumer fraud and/or other claims, including civil and criminal governmental actions, require it to make significant provisions in its accounts relating to legal proceedings and could materially adversely affect the Issuer's financial condition or results of operations, particularly where such circumstances are not covered by insurance.

Adverse outcome of litigation and/or governmental investigations

The Issuer may be subject to various product liability, consumer, commercial, anti-trust, environmental, employment or tax litigation or other legal proceedings and governmental investigations. Litigation, particularly in the US, is inherently unpredictable and unexpectedly high awards for damages can result from an adverse verdict. In many cases, plaintiffs may claim enhanced damages in extremely high amounts. In particular, the marketing, promotional, clinical and pricing practices of pharmaceutical manufacturers, as well as the manner in which manufacturers interact with purchasers, prescribers and patients, are subject to extensive regulation, litigation and governmental investigation. Many companies, including the Issuer, have been subject to claims related to these practices asserted by federal and state governmental authorities and private payers and consumers, which have resulted in substantial expense and other significant consequences.

Governmental investigations, for example under the US Foreign Corrupt Practices Act or federal or state False Claims Acts or other types of legal proceedings, regardless of their outcome, could be costly, divert management attention, or damage the Issuer's reputation and demand for its products. Unfavourable resolution of current and similar future proceedings against the Issuer could subject it to criminal liability, fines, penalties or other monetary or non-monetary remedies, including enhanced damages, require it to make significant provisions in the Issuer's accounts relating to legal proceedings and could materially adversely affect its business or results of operations.

Failure to adhere to increasingly stringent anti-bribery and anti-corruption legislation

There remains an increased global focus on the implementation and enforcement of anti-bribery and anti-corruption legislation.

Two relevant pieces of legislation include the UK Bribery Act and the US Foreign Corrupt Practices Act, and many other countries where the Issuer operates are also enforcing their own laws more aggressively and/or adopting tougher new measures. There has also been an increase in co-operation and co-ordination between regulators across countries with respect to investigation and enforcement.

The Issuer has been the subject of anti-corruption investigations and there can be no assurance that it will not, from time to time, be subject to informal enquiries and formal investigations from governmental agencies. In the context of the Issuer's business, governmental officials interact with it in various roles that are important to its operations, such as in the capacity of a regulator, partner or healthcare payer, reimbursor or prescriber, amongst others.

Despite the Issuer taking measures to prevent breaches of applicable anti-bribery and anti-corruption laws by its personnel and associated third-parties, breaches may still occur, potentially resulting in the imposition of significant penalties, such as fines, the requirement to comply with monitoring or self-reporting obligations, or debarment or exclusion from government sales or reimbursement programmes, any of which could materially adversely affect the Issuer's reputation, business or results of operations.

Economic and Financial Risks

Failure to achieve strategic plans or to meet targets and expectations

From time to time, the Issuer communicates its business strategy or its targets or expectations regarding its future financial or other performance. All such statements are of a forward-looking nature and are based on assumptions and judgements the Issuer makes, all of which are subject to significant inherent risks and uncertainties, including those that it is unaware of and/or that are beyond its control.

There can be no guarantee that the Issuer's financial targets or expectations will materialise on the expected timeline or at all. Actual results may deviate materially and adversely from any such target or expectation, including if one or more of the assumptions or judgements underlying any such target or expectation proves to be incorrect in whole or in part.

Any failure to successfully implement the Issuer's business strategy, whether determined by internal or external risk factors, may frustrate the achievement of the Issuer's financial or other targets or expectations and, in turn, materially damage the Issuer's brand and materially adversely affect its business, financial position or results of operations.

Failure in financial control or the occurrence of fraud

Effective internal controls are necessary for the Issuer to provide reliable financial reports and are designed to prevent and detect fraud. Lapses in controls and procedures could undermine the ability to prevent fraud or provide accurate disclosure of financial information on a timely basis. Testing of the Issuer's internal controls can provide only reasonable assurance with respect to the preparation and fair presentation of financial statements and may not prevent or detect misstatements or fraud.

Significant resources may be required to remediate any lapse or deficiency in internal controls.

Any such deficiency may also trigger investigations by a number of organisations, for example, the SEC, the DOJ or the UK Serious Fraud Office and may result in fines being levied against the Group individual directors or officers.

Serious fraud may lead to potential prosecution or even imprisonment of senior management.

Unexpected deterioration in the Issuer's financial position

A wide range of financial risks could result in a material deterioration of the Group's financial position.

As a global business, currency fluctuations can significantly affect the Issuer's results of operations, which are reported in US dollars. Approximately 33 per cent. of the Group's global 2018 product sales were in the US, which is expected to remain its largest single market for the foreseeable future. Product sales in other countries are predominantly in currencies other than the US dollar, including Chinese renminbi, the euro, Japanese yen and pound sterling.

Movements in the exchange rates used to translate foreign currencies into US dollars may materially adversely affect the Issuer's financial condition or results of operations. Some of the Issuer's subsidiaries import and export goods and services in currencies other than their own functional currency, and so the financial results of such subsidiaries could be affected by currency fluctuations arising between the transaction and settlement dates. In addition, there are foreign exchange differences arising on the translation of investments in subsidiaries.

The Issuer's consolidated balance sheet contains significant investments in intangible assets, including goodwill. The nature of the pharmaceutical business is high risk and requires that the Issuer invests in a large number of projects in an effort to develop a successful portfolio of approved products. The Issuer's ability to realise value on these significant investments is often contingent upon, among other things, regulatory approvals, market acceptance, competition and legal developments. As such, in the course of the Issuer's many acquisitions and R&D activities, the Issuer expects that some of its intangible assets will become impaired and be written off at some time in the future. Impairment losses may materially adversely affect its financial condition or results of operations.

Inherent variability of biologics manufacturing increases the risk of write-offs of product batches of biologics medicines. Due to the value of the materials used, the carrying amount of biologic products is much higher than that of small molecule products. As the Issuer continues to grow its biologics business, it also increases the risk of potential impairment charges

The costs associated with product liability litigation have increased the cost of, and narrowed the coverage afforded by, pharmaceutical companies' product liability insurance. To contain insurance costs, as of February 2006, the Issuer adjusted its product liability coverage profile, accepting uninsured exposure above US\$100 million. In addition, where claims are made under insurance policies, insurers may reserve the right to deny coverage on various grounds. For example, product liability litigation cases relating to *Farxiga* and *Nexium* in the US are not covered by third-party product liability insurance.

Financial liabilities arising due to product liability or other litigation, in respect of which the Issuer does not have insurance coverage, or if an insurer's denial of coverage is ultimately upheld, could require the Issuer to

make significant provisions relating to legal proceedings and could materially adversely affect the Issuer's financial condition or results of operations.

The Group's worldwide operations are taxed under laws in the jurisdictions in which they operate. International standards governing the global tax environment regularly change. The Organisation for Economic Co-operation and Development ("OECD") has proposed a number of changes under the Base Erosion and Profit Shifting ("BEPS") Action Plans which are now being progressively implemented by tax authorities around the world.

The resolution of tax disputes regarding the profits to be taxed in individual territories can result in a reallocation of profits between jurisdictions and an increase or decrease in related tax costs, and has the potential to affect the Issuer's cash flows, earnings per share and post-tax earnings. Claims, regardless of their merits or their outcome, are costly, divert management attention and may adversely affect the Issuer's reputation.

The integrated nature of the Issuer's worldwide operations can produce conflicting claims from revenue authorities as to the profits to be taxed in individual countries. The majority of the jurisdictions in which the Issuer operates have double tax treaties with other foreign jurisdictions, which provide a framework for mitigating the incidence of double taxation on the Issuer's revenues and capital gains.

If any double tax treaties are withdrawn or amended, especially in a territory where a member of the Group is involved in a taxation dispute with a tax authority in relation to cross-border transactions, such withdrawal or amendment, could materially adversely affect the Issuer's financial condition or results of operations, as could a negative outcome of a tax dispute or a failure by tax authorities to agree through competent authority proceedings. Changes to the application of double tax treaties, as a result of the parent company of the Group no longer being an EU entity following Brexit, could also result in adverse consequences such as those described above.

Changes in tax regimes, such as those relating to the US federal tax regime which were effective from 1 January 2018, could result in a material impact on the Group's cash tax liabilities and tax charge, resulting in either an increase or a reduction in financial results depending upon the nature of the change. The Issuer represents views to the OECD, governments and tax authorities through public consultations to ensure international institutions and governments understand the business implications of proposed law changes. Specific OECD BEPS recommendations that the Group expects will impact it include changes to patent box regimes, restrictions of interest deductibility and revised transfer pricing guidelines.

The Issuer's defined benefit pension obligations are largely backed by assets invested across the broad investment market. The Issuer's most significant obligations relate to defined benefit pension funds in the UK, Sweden and the US. The largest obligation is in the UK.

Sustained falls in asset values could reduce pension fund solvency levels, which may result in requirements for additional cash, restricting the cash available for the Issuer's business. Changes to funding regulations for defined benefit pensions may also result in a requirement for additional cash contributions by the Group. If the present value of the liabilities increases due to a sustained low interest rate environment, an increase in expectations of future inflation, or an improvement in member longevity (above that already assumed), this could also reduce pension fund solvency ratios. The likely increase in the IAS 19 accounting deficit generated by any of these factors may cause the credit rating agencies to review the Issuer's credit rating, with the potential to negatively affect its ability to raise debt and the price of new debt issuances.

RISK RELATING TO THE NOTES

There is no active trading market for the Notes

Notes issued under the Programme will be new securities which may not be widely distributed and for which there is currently no active trading market (unless in the case of any particular Tranche, such Tranche is to be consolidated with and form a single series with a Tranche of Notes which is already issued). If the Notes are traded after their initial issuance, they may trade at a discount to their initial offering price, depending upon prevailing interest rates, the market for similar securities, general economic conditions and the financial condition of the Issuer. Although applications have been made for the Notes issued under the Programme to be admitted to the Official List of the FCA and to trading on the Regulated Market of the London Stock Exchange, there is no assurance that such applications will be accepted, that any particular Tranche of Notes

will be so admitted or that an active trading market will develop. Accordingly, there is no assurance as to the development or liquidity of any trading market for any particular Tranche of Notes.

Global economic conditions

Holders of Notes should be aware that adverse changes in the global credit markets may adversely affect the borrowing capacity and the cost of borrowing of the Issuer. In addition, holders of Notes should be aware that, in view of the prevailing and widely reported global credit market conditions (which continue at the date hereof), the secondary market for Notes and instruments of this kind may be illiquid. The Issuer cannot predict when these circumstances will change.

Interest rate risks

Investment in fixed rate Notes involves the risk that subsequent changes in market interest rates may adversely affect the value of fixed rate Notes.

The Notes may be redeemed prior to maturity

In the event that the Issuer would be obliged to increase the amounts payable in respect of any Notes due to any withholding or deduction for or on account of, any present or future taxes, duties, assessments or governmental charges of whatever nature imposed, levied, collected, withheld or assessed by or on behalf of the United Kingdom or any political subdivision thereof or any authority therein or thereof having power to tax, the Issuer may redeem all outstanding Notes in accordance with the Conditions.

In addition, if in the case of any particular Tranche of Notes the relevant Final Terms specify that the Notes are redeemable at the Issuer's option in certain other circumstances the Issuer may choose to redeem the Notes at times when prevailing interest rates may be relatively low. In such circumstances an investor may not be able to reinvest the redemption proceeds in a comparable security at an effective interest rate as high as that of the relevant Notes.

Because the Global Notes are held by or on behalf of Euroclear and Clearstream, or lodged with a sub-custodian for CMU, investors will have to rely on their procedures for transfers, payments and communications with the Issuer

Notes issued under the Programme may be represented by one or more Global Notes. Such Global Notes will be deposited with a common depository or, as the case may be, common safekeeper for Euroclear Bank SA/NV ("**Euroclear**") and Clearstream Banking S.A. ("**Clearstream**") or lodged with a sub-custodian for CMU. Except in the circumstances described in the relevant Global Note, investors will not be entitled to receive Definitive Notes. The relevant clearing system(s) will maintain records of the beneficial interests in the Global Notes. While the Notes are represented by one or more Global Notes, investors will be able to trade their beneficial interests only through the clearing system(s).

While the Notes are represented by one or more Global Notes the Issuer will discharge its payment obligations under the Notes by making payments to the common depository or, as the case may be, a common safekeeper for Euroclear and Clearstream or, as the case may be, a sub-custodian for CMU, for distribution to their account holders. A holder of a beneficial interest in a Global Note must rely on the procedures of Euroclear and Clearstream or, as the case may be, CMU to receive payments under the relevant Notes. The Issuer has no responsibility or liability for the records relating to, or payments made in respect of, beneficial interests in the Global Notes.

Holders of beneficial interests in the Global Notes will not have a direct right to vote in respect of the relevant Notes. Instead, such holders will be permitted to act only to the extent that they are enabled by the relevant clearing system(s) to appoint appropriate proxies.

Modification, waivers and substitution

The Conditions contain provisions for calling meetings of Noteholders to consider matters affecting their interests generally. These provisions permit defined majorities to bind all Noteholders including Noteholders who did not attend and vote at the relevant meeting and Noteholders who voted in a manner contrary to the majority.

The Conditions also provide that the Trustee may, without the consent of Noteholders, agree to (i) any modification of, or to the waiver or authorisation of any breach or proposed breach of, any of the provisions of Notes or (ii) determine without the consent of the Noteholders that any Event of Default or potential Event of Default shall not be treated as such.

Notes with integral multiples

In relation to any issue of Notes which have a denomination consisting of the minimum Specified Denomination plus a higher integral multiple of another smaller amount, it is possible that the Notes may be traded in amounts in excess of the Specified Denomination that are not integral multiples of the Specified Denomination. Noteholders who, as a result of trading such amounts, hold a principal amount of Notes other than a multiple of the minimum Specified Denomination will receive definitive Notes in respect of their holding (provided that the aggregate amount of Notes they hold is in excess of the minimum Specified Denomination), however, any such definitive Notes which are printed in denominations other than the minimum Specified Denomination may be illiquid and difficult to trade. Furthermore, a Noteholder who, as a result of trading such amounts, holds a principal amount of less than the minimum Specified Denomination may not receive a definitive Note in respect of such holding (should definitive Notes be printed) and would need to purchase a principal amount of Notes such that its holding amounts to a Specified Denomination.

If an investor holds Notes which are not denominated in the investor's home currency, he will be exposed to movements in exchange rates adversely affecting the value of his holding. In addition, the imposition of exchange controls in relation to any Notes could result in an investor not receiving payments on those Notes

The Issuer will pay principal and interest on the Notes in the Specified Currency. This presents certain risks relating to currency conversions if an investor's financial activities are denominated principally in a currency or currency unit (the "**Investor's Currency**") other than the Specified Currency. These include the risk that exchange rates may significantly change (including changes due to devaluation of the Specified Currency or revaluation of the Investor's Currency) and the risk that authorities with jurisdiction over the Investor's Currency may impose or modify exchange controls. An appreciation in the value of the Investor's Currency relative to the Specified Currency would decrease (1) the Investor's Currency-equivalent yield on the Notes, (2) the Investor's Currency-equivalent value of the principal payable on the Notes and (3) the Investor's Currency-equivalent market value of the Notes.

Government and monetary authorities may impose (as some have done in the past) exchange controls that could adversely affect an applicable exchange rate or the ability of the Issuer to make payments in respect of the Notes. As a result, investors may receive less interest or principal than expected, or no interest or principal.

Credit ratings may not reflect all risks and may affect the trading price of the Notes

Tranches of Notes that may be issued under the Programme may be rated or unrated. Where a Tranche of Notes issued under the Programme is rated, the applicable rating(s) will be specified in the relevant Final Terms. Such rating will not necessarily be the same as the rating(s) assigned to the Programme, the Issuer or to Notes already issued. One or more independent credit rating agencies may also assign credit ratings to the Notes.

Such ratings may not reflect the potential impact of all risks discussed above, and other factors that may affect the value of any Tranche of Notes. In addition, any negative change in the credit ratings of the Issuer could adversely affect the trading price of the Notes. A credit rating is not a recommendation to buy, sell or hold securities and may be revised or withdrawn by the relevant rating agency at any time.

Notes denominated in Renminbi are subject to additional risks

Set out below is a description of the principal risks which may be relevant to an investor in Notes denominated in Renminbi ("**Renminbi Notes**"):

Renminbi is not freely convertible and there are significant restrictions on the remittance of Renminbi into and out of the PRC which may adversely affect the liquidity of Renminbi Notes

Renminbi is not freely convertible at present. The government of the PRC (the "**PRC Government**") continues to regulate conversion between Renminbi and foreign currencies, including the Hong Kong dollar.

However, there has been significant reduction in control by the PRC Government in recent years, particularly over trade transactions involving import and export of goods and services as well as other frequent routine foreign exchange transactions. These transactions are known as current account items.

On the other hand, remittance of Renminbi into and out of the PRC for the settlement of capital account items, such as capital contributions, debt financing and securities investment, is generally only permitted upon obtaining specific approvals from, or completing specific registrations or filings with, the relevant authorities and/or designated foreign exchange banks on a case-by-case basis and is subject to a strict monitoring system. Regulations in the PRC on the remittance of Renminbi into and out of the PRC for settlement of capital account items are being developed.

Although Renminbi was added to the Special Drawing Rights basket created by the International Monetary Fund in 2016 and policies further improving accessibility to Renminbi to settle cross-border transactions in foreign currencies were implemented by the People's Bank of China ("**PBoC**") in 2018, there is no assurance that the PRC Government will continue to gradually liberalise control over cross-border remittance of Renminbi in the future, that the schemes for Renminbi cross-border utilisation will not be discontinued or that new regulations in the PRC will not be promulgated in the future which have the effect of restricting or eliminating the remittance of Renminbi into or out of the PRC. Despite the Renminbi internationalisation pilot programme and efforts in recent years to internationalise the currency, there can be no assurance that the PRC Government will not impose interim or long-term restrictions on the crossborder remittance of Renminbi. In the event that funds cannot be repatriated out of the PRC in Renminbi, this may affect the overall availability of Renminbi outside the PRC and the ability of the Issuer to source Renminbi to finance its obligations under Notes denominated in Renminbi.

There is only limited availability of Renminbi outside the PRC, which may affect the liquidity of the Renminbi Notes and the Issuer's ability to source Renminbi outside the PRC to service Renminbi Notes

As a result of the restrictions by the PRC Government on cross-border Renminbi fund flows, the availability of Renminbi outside the PRC is limited. The PBoC has entered into agreements (the "**Settlement Arrangements**") on the clearing of Renminbi business with financial institutions (the "**Renminbi Clearing Banks**") in a number of financial centres and cities, including but not limited to Hong Kong, has established the Cross-Border Inter-Bank Payments System (CIPS) to facilitate cross-border Renminbi settlement, and is in the process of establishing Renminbi clearing and settlement mechanisms in several other jurisdictions. Nevertheless, the current size of Renminbi denominated financial assets outside the PRC is limited.

There are restrictions imposed by PBoC on Renminbi business participating banks in respect of cross-border Renminbi settlement, such as those relating to direct transactions with PRC enterprises. Furthermore, Renminbi business participating banks do not have direct Renminbi liquidity support from PBoC, although PBoC has gradually allowed participating banks to access the PRC's onshore inter-bank market for trading of Renminbi. The Renminbi Clearing Banks only have limited access to onshore liquidity support from PBoC for the purpose of squaring open positions of participating banks for limited types of transactions and are not obliged to square for participating banks any open positions resulting from other foreign exchange transactions or conversion services. In cases where the participating banks cannot source sufficient Renminbi through the above channels, they will need to source Renminbi from outside the PRC to square such open positions.

Although it is expected that the offshore Renminbi market will continue to grow in depth and size, its growth is subject to many constraints as a result of PRC laws and regulations on foreign exchange. There is no assurance that new PRC regulations will not be promulgated or the Settlement Arrangements will not be terminated or amended in the future which will have the effect of restricting availability of Renminbi outside the PRC. The limited availability of Renminbi outside the PRC may affect the liquidity of the Renminbi Notes. To the extent the Issuer is required to source Renminbi in the offshore market to service its Renminbi Notes, there is no assurance that the Issuer will be able to source such Renminbi on satisfactory terms, if at all.

Payments with respect to the Renminbi Notes may be made only in the manner designated in the Renminbi Notes

All payments to investors in respect of the Renminbi Notes will be made solely (i) for so long as the Renminbi Notes are represented by global certificates held with the common depositary or common safekeeper, as the case may be, for Clearstream and Euroclear or any alternative clearing system, by transfer to a Renminbi bank account maintained in Hong Kong or a financial centre in which a Renminbi Clearing Bank clears and settles Renminbi, (ii) for so long as the Renminbi Notes are represented by global certificates lodged with a sub-

custodian for or registered with the CMU, by transfer to a Renminbi bank account maintained in Hong Kong in accordance with prevailing CMU rules and procedures, or (iii) for so long as the Renminbi Notes are in definitive form, by transfer to a Renminbi bank account maintained in Hong Kong or a financial centre in which a Renminbi Clearing Bank clears and settles Renminbi in accordance with prevailing rules and regulations. The Issuer cannot be required to make payment by any other means (including in any other currency or by transfer to a bank account in the PRC).

Gains on the transfer of the Renminbi Notes may become subject to income taxes under PRC tax laws

Under the PRC Enterprise Income Tax Law, the PRC Individual Income Tax Law and the relevant implementing rules, as amended from time to time, any gain realised on the transfer of Renminbi Notes by non-PRC resident enterprise or individual Noteholders may be subject to PRC enterprise income tax ("EIT") or PRC individual income tax ("IIT") if such gain is regarded as income derived from sources within the PRC. The PRC Enterprise Income Tax Law levies EIT at the rate of 20 per cent. of the gains derived by such non-PRC resident enterprise Noteholder from the transfer of Renminbi Notes but its implementation rules have reduced the enterprise income tax rate to 10 per cent. The PRC Individual Income Tax Law levies IIT at a rate of 20 per cent. of the gains derived by non-PRC resident individual Noteholders from the transfer of Renminbi Notes.

However, uncertainty remains as to whether the gain realised from the transfer of Renminbi Notes by non-PRC resident enterprise or individual Noteholders would be treated as income derived from sources within the PRC and become subject to the EIT or IIT. This will depend on how the PRC tax authorities interpret, apply or enforce the PRC Enterprise Income Tax Law, the PRC Individual Income Tax Law and the relevant implementing rules. According to the arrangement between the PRC and Hong Kong, for avoidance of double taxation, Noteholders who are residents of Hong Kong, including enterprise Noteholders and individual Noteholders, will not be subject to EIT or IIT on capital gains derived from a sale or exchange of the Notes.

Therefore, if non-PRC resident enterprise or individual Noteholders are required to pay PRC income tax on gains derived from the transfer of Renminbi Notes, unless there is an applicable tax treaty between PRC and the jurisdiction in which such non-PRC resident enterprise or individual holders of Renminbi Notes reside that reduces or exempts the relevant EIT or IIT, the value of their investment in Renminbi Notes may be materially and adversely affected.

Investment in the Renminbi Notes is subject to currency risk

If the Issuer is not able, or it is impracticable for it, to satisfy its obligation to pay interest and principal on the Renminbi Notes as a result of Inconvertibility, Non-transferability or Illiquidity (each, as defined in the Conditions), the Issuer shall be entitled, on giving not less than 10 Hong Kong Banking Days' nor more than 30 calendar days' irrevocable notice to the investors prior to the due date for payment, to settle any such payment in U.S. Dollars on the due date at the U.S. Dollar Equivalent (as defined in the Conditions) of any such interest or principal, as the case may be.

Investment in the Renminbi Notes is subject to exchange rate risks

The value of Renminbi against other foreign currencies fluctuates from time to time and is affected by changes in the PRC and international political and economic conditions as well as many other factors. Recently, the PBoC implemented changes to the way the Renminbi's daily mid-point against the U.S. dollar is determined, by requesting market-makers to submit daily mid-point quotations by reference to the closing rate on the inter-banks market of the previous day. This change, and others that may be implemented, may increase the volatility in the value of the Renminbi against foreign currencies. All payments of interest and principal will be made in Renminbi with respect to Renminbi Notes unless otherwise specified. As a result, the value of these Renminbi payments may vary with the changes in the prevailing exchange rates in the marketplace. If the value of Renminbi depreciates against another foreign currency, the value of the investment made by a holder of the Renminbi Notes in that foreign currency will decline.

Investment in the Renminbi Notes is subject to interest rate risks

The PRC Government has gradually liberalised its regulation of interest rates in recent years. Further liberalisation may increase interest rate volatility. In addition, the interest rate for Renminbi in markets outside the PRC may significantly deviate from the interest rate for Renminbi in the PRC as a result of foreign exchange controls imposed by PRC law and regulations and prevailing market conditions.

As Renminbi Notes may carry a fixed interest rate, the trading price of the Renminbi Notes will consequently vary with the fluctuations in the Renminbi interest rates. If holders of the Renminbi Notes propose to sell their Renminbi Notes before their maturity, they may receive an offer lower than the amount they have invested.

Foreign Account Tax Compliance withholding

The Issuer does not believe that payments under the Notes will be subject to withholding tax under sections 1471 through 1474 of the U.S. Internal Revenue Code, certain intergovernmental agreements relating thereto and laws implementing to the foregoing (collectively "**FATCA**"). FATCA imposes a new reporting regime and, potentially, a 30 per cent. withholding tax with respect to (i) certain payments from sources within the United States, and (ii) "foreign passthru payments" made by certain non-U.S. financial institutions to certain other non-U.S. financial institutions that do not comply with this new reporting regime. The Issuer does not expect to be considered a financial institution, or for payments on the Notes to be considered from sources in the United States and accordingly, no payments under the Notes should be subject to withholding under FATCA. If, contrary to expectations, FATCA withholding were imposed on any payments under the Notes, no additional amounts or other compensation would be paid in respect of such withholding.

There are risks that certain benchmark rates may be administered differently or discontinued in the future, including the potential phasing-out of LIBOR after 2021, which may adversely affect the trading market for, value of and return on, Notes based on such benchmarks

The London Interbank Offered Rate ("**LIBOR**"), the Euro Interbank Offered Rate ("**EURIBOR**") and other interest rate or other types of rates and indices which are deemed to be benchmarks are the subject of ongoing national and international regulatory discussions and proposals for reform. Some of these reforms are already effective whilst others are still to be implemented.

The Benchmarks Regulation on indices used as benchmarks in financial instruments and financial contracts or to measure the performance of investment funds was published in the Official Journal of the EU on 29 June 2016 and became applicable from 1 January 2018. The Benchmarks Regulation applies to the provision of benchmarks, the contribution of input data to a benchmark and the use of a benchmark, within the EU. It will, among other things, (i) require benchmark administrators to be authorised or registered (or, if non-EU-based, to be subject to an equivalent regime or otherwise recognised or endorsed) and (ii) prevent certain uses by EU supervised entities of benchmarks of administrators that are not authorised or registered (or, if non-EU based, not deemed equivalent or recognised or endorsed).

The Benchmark Regulation could have a material impact on any Notes linked to LIBOR, EURIBOR or another benchmark rate or index, in particular, if the methodology or other terms of the benchmark are changed in order to comply with the terms of the Benchmark Regulation, and such changes could (amongst other things) have the effect of reducing or increasing the rate or level, or affecting the volatility of the published rate or level, of the benchmark.

More broadly, any of the international, national or other proposals for reform, or the general increased regulatory scrutiny of benchmarks, could increase the costs and risks of administering or otherwise participating in the setting of a benchmark and complying with any such regulations or requirements. Such factors may have the following effects on certain benchmarks: (i) discourage market participants from continuing to administer or contribute to such benchmark; (ii) trigger changes in the rules or methodologies used in the benchmarks or (iii) lead to the disappearance of the benchmark.

As an example of such benchmark reforms on 27 July 2017, the UK Financial Conduct Authority announced that it will no longer persuade or compel banks to submit rates for the calculation of the LIBOR benchmark after 2021 (the "**2017 FCA Announcement**"). On 12 July 2018, the FCA further announced that the LIBOR benchmark may cease to be a regulated benchmark under the Benchmark Regulation (the "**2018 FCA Announcement**"). The 2017 FCA Announcement and the 2018 FCA Announcement indicate that the continuation of LIBOR on the current basis (or at all) cannot and will not be guaranteed after 2021.

At this time, it is not possible to predict the effect of any establishment of alternative reference rates or any other reforms to LIBOR that may be enacted in the United Kingdom or elsewhere. Uncertainty as to the nature of such alternative reference rates or other reforms may adversely affect the trading market for LIBOR-linked securities. The potential elimination of benchmarks, such as LIBOR, the establishment of alternative reference rates or changes in the manner of administration of a benchmark could also require adjustments to the terms of benchmark-linked securities and may result in other consequences, such as interest payments that are lower

than, or that do not otherwise correlate over time with, the payments that would have been made on those securities if the relevant benchmark was available in its current form.

The elimination of the LIBOR benchmark or any other benchmark, or changes in the manner of administration of any benchmark, could require or result in an adjustment to the interest calculation provisions of the Conditions (as further described in Condition 7(i) (*Benchmark Discontinuation*)), or result in adverse consequences to holders of any Notes linked to such benchmark (including Floating Rate Notes whose interest rates are linked to LIBOR, EURIBOR or any other such benchmark that is subject to reform). Furthermore, even prior to the implementation of any changes, uncertainty as to the nature of alternative reference rates and as to potential changes to such benchmark may adversely affect such benchmark during the term of the relevant Notes, the return on the relevant Notes and the trading market for securities (including the Notes) based on the same benchmark.

The "*Terms and Conditions of the Notes*" provide for certain fallback arrangements in the event that a published benchmark, such as LIBOR, (including any page on which such benchmark may be published (or any successor service)) becomes unavailable, including the possibility that the rate of interest could be set by reference to a successor rate or an alternative rate and that such successor rate or alternative reference rate may be adjusted (if required) in order to reduce or eliminate, to the extent reasonably practicable in the circumstances, any economic prejudice or benefit (as applicable) to investors arising out of the replacement of the relevant benchmark, although the application of such adjustments to the Notes may not achieve this objective. Any such changes may result in the Notes performing differently (which may include payment of a lower interest rate) than if the original benchmark continued to apply. In certain circumstances the ultimate fallback of interest for a particular Interest Period may result in the rate of interest for the last preceding Interest Period being used. This may result in the effective application of a fixed rate for Floating Rate Notes based on the rate which was last observed on the Relevant Screen Page. In addition, due to the uncertainty concerning the availability of successor rates and alternative reference rates and the involvement of an Independent Adviser (as defined in the Conditions), the relevant fallback provisions may not operate as intended at the relevant time.

Any such consequences could have a material adverse effect on the value of and return on any such Notes. Investors should consult their own independent advisers and make their own assessment about the potential risks imposed by the Benchmark Regulation reforms in making any investment decision with respect to any Notes linked to or referencing a benchmark.

DOCUMENTS INCORPORATED BY REFERENCE

The following documents (excluding all information incorporated by reference in any such documents either expressly or implicitly and excluding any information or statements included in any such documents either expressly or implicitly that is or might be considered to be forward looking) shall be deemed to be incorporated by reference in, and to form part of, this Base Prospectus:

- pages 44 to 59 of the unaudited "Q1 2019 Results" of the Issuer as at and for the 3 months ended 31 March 2019;
- pages 144 to 200 of the "Annual Report and Form 20-F Information 2018" of the Issuer (the audited consolidated financial statements of the Issuer as at and for the year ended 31 December 2018 together with the notes thereto and the independent auditor's report to the members of AstraZeneca PLC (Group));
- pages 129 to 193 of the "Annual Report and Form 20-F Information 2017" of the Issuer (the audited consolidated financial statements of the Issuer as at and for the year ended 31 December 2017 together with the notes thereto and the independent auditor's report to the members of AstraZeneca PLC (Group)); and
- the Terms and Conditions of the Notes as set out on pages 31 to 57 (inclusive) of the base prospectus dated 5 May 2016 relating to the Programme.

Any non-incorporated parts of a document referred to herein are either deemed not relevant for an investor or are otherwise covered elsewhere in this Base Prospectus.

Copies of the documents incorporated by reference in this Base Prospectus may be inspected, free of charge, at the specified office in London of the Principal Paying Agent and will be available to the public on the Issuer's website (www.astrazeneca.com/Investors).

FINAL TERMS AND DRAWDOWN PROSPECTUSES

In this section the expression "**necessary information**" means, in relation to any Tranche of Notes, the information necessary to enable investors to make an informed assessment of the assets and liabilities, financial position, profits and losses and prospects of the Issuer and of the rights attaching to the Notes. In relation to the different types of Notes which may be issued under the Programme the Issuer has included in this Base Prospectus all of the necessary information except for information relating to the Notes which is not known at the date of this Base Prospectus and which can only be determined at the time of an individual issue of a Tranche of Notes.

Any information relating to the Notes which is not included in this Base Prospectus and which is required in order to complete the necessary information in relation to a Tranche of Notes will be contained either in the relevant Final Terms or in a Drawdown Prospectus. Such information will be contained in the relevant Final Terms unless any of such information constitutes a significant new factor relating to the information contained in this Base Prospectus in which case such information, together with all of the other necessary information in relation to the relevant series of Notes, may be contained in a Drawdown Prospectus.

For a Tranche of Notes which is the subject of Final Terms, those Final Terms will, for the purposes of that Tranche only, complete this Base Prospectus and must be read in conjunction with this Base Prospectus. The terms and conditions applicable to any particular Tranche of Notes which is the subject of Final Terms are the Conditions as completed to the extent described in the relevant Final Terms.

The terms and conditions applicable to any particular Tranche of Notes which is the subject of a Drawdown Prospectus will be the Conditions as supplemented, amended and/or replaced to the extent described in the relevant Drawdown Prospectus. In the case of a Tranche of Notes which is the subject of a Drawdown Prospectus, each reference in this Base Prospectus to information being specified or identified in the relevant Final Terms shall be read and construed as a reference to such information being specified or identified in the relevant Drawdown Prospectus unless the context requires otherwise.

The Issuer will, in the event of any significant new factor, material mistake or inaccuracy relating to information included in this Base Prospectus which is capable of affecting the assessment of any Notes, prepare a supplement to this Base Prospectus or publish a new Base Prospectus for use in connection with any subsequent issue of Notes.

FORMS OF NOTES

Each Tranche of Notes will initially be in the form of either a temporary global note (the "**Temporary Global Note**"), without interest coupons, or a permanent global note (the "**Permanent Global Note**"), without interest coupons, in each case as specified in the relevant Final Terms. Each Temporary Global Note or, as the case may be, Permanent Global Note (each a "**Global Note**") which is not intended to be issued in new global note ("**NGN**") form, as specified in the relevant Final Terms, will, on or around the issue date of the relevant Tranche of the Notes, be deposited with a depository or a common depository for Euroclear Bank SA/NV ("**Euroclear**") and/or Clearstream Banking S.A. ("**Clearstream**") or lodged with a sub-custodian for the Central Moneymarkets Unit Service operated by the Hong Kong Monetary Authority ("**CMU**", and together with Euroclear and Clearstream, the "**Clearing Systems**") and/or any other relevant clearing system and each Global Note which is intended to be issued in NGN form, as specified in the relevant Final Terms, will, on or around the issue date of the relevant Tranche of the Notes, be deposited with a common safekeeper for Euroclear and/or Clearstream.

On 13 June 2006, the European Central Bank (the "**ECB**") announced that Notes in NGN form are in compliance with the "Standards for the use of EU securities settlement systems in ESCB credit operations" of the central banking system for the euro (the "**Eurosystem**"), **provided that** certain other criteria are fulfilled. At the same time the ECB also announced that arrangements for Notes in NGN form will be offered by Euroclear and Clearstream as of 30 June 2006 and that debt securities in global bearer form issued through Euroclear and Clearstream after 31 December 2006 will only be eligible as collateral for Eurosystem operations if the NGN form is used.

The relevant Final Terms will also specify whether United States Treasury Regulation §1.163-5(c)(2)(i)(C) (the "**TEFRA C Rules**") or United States Treasury Regulation §1.163-5(c)(2)(i)(D) (the "**TEFRA D Rules**") are applicable in relation to the Notes or, if the Notes do not have a maturity of more than 365 days, that neither the TEFRA C Rules nor the TEFRA D Rules are applicable.

Temporary Global Note exchangeable for Permanent Global Note

If the relevant Final Terms specifies the form of Notes as being "Temporary Global Note exchangeable for a Permanent Global Note", then the Notes will initially be in the form of a Temporary Global Note which will be exchangeable, in whole or in part, for interests in a Permanent Global Note, without interest coupons, from the 40th day after the issue date of the relevant Tranche of the Notes upon certification as to non-U.S. beneficial ownership. No payments will be made under the Temporary Global Note unless exchange for interests in the Permanent Global Note is improperly withheld or refused. In addition, interest payments in respect of the Notes cannot be collected without such certification of non-U.S. beneficial ownership.

Whenever any interest in the Temporary Global Note is to be exchanged for an interest in a Permanent Global Note, the Issuer shall procure (in the case of first exchange) the prompt delivery (free of charge to the bearer) of such Permanent Global Note to the bearer of the Temporary Global Note or (in the case of any subsequent exchange) an increase in the principal amount of the Permanent Global Note in accordance with its terms against:

- (i) presentation and (in the case of final exchange) surrender of the Temporary Global Note to or to the order of the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent; and
- (ii) receipt by the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent of a certificate or certificates of non-U.S. beneficial ownership,

within 7 days of the bearer requesting such exchange.

The principal amount of the Permanent Global Note shall be equal to the aggregate of the principal amounts specified in the certificates of non-U.S. beneficial ownership; **provided, however, that** in no circumstances shall the principal amount of the Permanent Global Note exceed the initial principal amount of the Temporary Global Note.

The Permanent Global Note will be exchangeable in whole, but not in part, for Notes in definitive form ("**Definitive Notes**"):

- (i) on the expiry of such period of notice as may be specified in the relevant Final Terms; or

- (ii) at any time, if so specified in the relevant Final Terms; or
- (iii) if the relevant Final Terms specifies "in the limited circumstances described in the Permanent Global Note", then if (a) Euroclear, Clearstream or CMU or any other relevant clearing system is closed for business for a continuous period of 14 days (other than by reason of legal holidays) or announces an intention permanently to cease business or (b) any of the circumstances described in Condition 12 (*Events of Default*) occurs.

For the avoidance of doubt, Notes will only be issued with a minimum Specified Denomination and in integral multiples of another smaller amount in excess thereof if the relevant Final Terms specifies "in the limited circumstances described in the Permanent Global Note" in accordance with paragraph (iii) above.

Whenever the Permanent Global Note is to be exchanged for Definitive Notes, the Issuer shall procure the prompt delivery (free of charge to the bearer) of such Definitive Notes, duly authenticated and with Coupons and Talons attached (if so specified in the relevant Final Terms), in an aggregate principal amount equal to the principal amount of the Permanent Global Note to the bearer of the Permanent Global Note against the surrender of the Permanent Global Note to or to the order of the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent within 30 days of the bearer requesting such exchange.

Temporary Global Note exchangeable for Definitive Notes

If the relevant Final Terms specifies the form of Notes as being "Temporary Global Note exchangeable for Definitive Notes" and also specifies that the TEFRA C Rules are applicable or that neither the TEFRA C Rules or the TEFRA D Rules are applicable, then the Notes will initially be in the form of a Temporary Global Note which will be exchangeable, in whole but not in part, for Definitive Notes from the 40th day after the issue date of the relevant Tranche of the Notes.

If the relevant Final Terms specifies the form of Notes as being "Temporary Global Note exchangeable for Definitive Notes" and also specifies that the TEFRA D Rules are applicable, then the Notes will initially be in the form of a Temporary Global Note which will be exchangeable, in whole or in part, for Definitive Notes from the 40th day after the issue date of the relevant Tranche of the Notes upon certification as to non-U.S. beneficial ownership. Interest payments in respect of the Notes cannot be collected without such certification of non-U.S. beneficial ownership.

Whenever the Temporary Global Note is to be exchanged for Definitive Notes, the Issuer shall procure the prompt delivery (free of charge to the bearer) of such Definitive Notes, duly authenticated and with Coupons and Talons attached (if so specified in the relevant Final Terms), in an aggregate principal amount equal to the principal amount of the Temporary Global Note to the bearer of the Temporary Global Note against the surrender of the Temporary Global Note to or to the order of the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent within 30 days of the bearer requesting such exchange.

For the avoidance of doubt, if Notes are to be issued with a minimum Specified Denomination and in integral multiples of another smaller amount in excess thereof as specified in the relevant Final Terms, the Notes cannot be represented on issue by a Temporary Global Note exchangeable for Definitive Notes.

Permanent Global Note exchangeable for Definitive Notes

If the relevant Final Terms specifies the form of Notes as being "Permanent Global Note exchangeable for Definitive Notes", then the Notes will initially be in the form of a Permanent Global Note which will be exchangeable in whole, but not in part, for Definitive Notes:

- (i) on the expiry of such period of notice as may be specified in the relevant Final Terms; or
- (ii) at any time, if so specified in the relevant Final Terms; or
- (iii) if the relevant Final Terms specifies "in the limited circumstances described in the Permanent Global Note", then if (a) Euroclear, Clearstream or CMU or any other relevant clearing system is closed for business for a continuous period of 14 days (other than by reason of legal holidays) or announces an intention permanently to cease business or does in fact do so and no other clearing system acceptable to the Trustee is then in existence or (b) any of the circumstances described in Condition 12 (*Events of Default*) occurs.

Whenever the Permanent Global Note is to be exchanged for Definitive Notes, the Issuer shall procure the prompt delivery (free of charge to the bearer) of such Definitive Notes, duly authenticated and with Coupons and Talons attached (if so specified in the relevant Final Terms), in an aggregate principal amount equal to the principal amount of the Permanent Global Note to the bearer of the Permanent Global Note against the surrender of the Permanent Global Note to or to the order of the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent within 30 days of the bearer requesting such exchange.

For the avoidance of doubt, Notes will only be issued with a minimum Specified Denomination and in integral multiples of another smaller amount in excess thereof if the relevant Final Terms specifies "in the limited circumstances described in the Permanent Global Note".

Terms and Conditions applicable to the Notes

The terms and conditions applicable to any Definitive Note will be endorsed on that Note and will consist of the terms and conditions set out under "*Terms and Conditions of the Notes*" below and the provisions of the relevant Final Terms which complete those terms and conditions.

The terms and conditions applicable to any Note in global form will differ from those terms and conditions which would apply to the Note were it in definitive form to the extent described under "*Summary of Provisions Relating to the Notes while in Global Form*" below.

Legend concerning United States persons

In the case of any Tranche of Notes having a maturity of more than 365 days, the Notes in global form, the Notes in definitive form and any Coupons and Talons appertaining thereto will bear the following legend:

"Any United States person who holds this obligation will be subject to limitations under the United States income tax laws, including the limitations provided in Sections 165(j) and 1287(a) of the Internal Revenue Code."

TERMS AND CONDITIONS OF THE NOTES

The following is the text of the terms and conditions which, as completed by the relevant Final Terms, will be endorsed on each Note in definitive form issued under the Programme. The terms and conditions applicable to any Note in global form will differ from those terms and conditions which would apply to the Note were it in definitive form to the extent described under "Summary of Provisions Relating to the Notes while in Global Form" below.

1. Introduction

(a) **Programme:**

AstraZeneca PLC (the "**Issuer**") has established a Euro Medium Term Note Programme (the "**Programme**") for the issuance of up to US\$10,000,000,000 in aggregate principal amount of notes (the "**Notes**").

(b) **Final Terms:**

Notes issued under the Programme are issued in series (each a "**Series**") and each Series may comprise one or more tranches (each a "**Tranche**") of Notes. Each Tranche is the subject of final terms (the "**Final Terms**") which completes these terms and conditions (the "**Conditions**"). The terms and conditions applicable to any particular Tranche of Notes are these Conditions as completed by the relevant Final Terms. In the event of any inconsistency between these Conditions and the relevant Final Terms, the relevant Final Terms shall prevail.

(c) **Trust Deed:**

The Notes are constituted by, have the benefit of and are in all respects subject to a trust deed made on 10 September 2007 and amended and restated on 12 June 2019 (the "**Trust Deed**") between the Issuer and Deutsche Trustee Company Limited (the "**Trustee**", which expression shall include all persons for the time being the trustee or trustees under the Trust Deed) as trustee for the Noteholders (as defined below).

(d) **Agency Agreement:**

The Notes are the subject of an amended and restated issue and paying agency agreement dated 12 June 2019 (the "**Agency Agreement**") between the Issuer, Deutsche Bank AG, London Branch as principal paying agent (the "**Principal Paying Agent**", which expression includes any successor principal paying agent appointed from time to time in connection with the Notes) and Deutsche Bank AG, Hong Kong Branch as CMU lodging and paying agent (the "**CMU Lodging and Paying Agent**", which expression includes any successor CMU lodging and paying agent appointed from time to time in connection with the Notes).

(e) **The Notes:**

All subsequent references in these Conditions to "Notes" are to the Notes which are the subject of the relevant Final Terms. Copies of the relevant Final Terms are available for viewing during normal business hours and copies may be obtained from the Specified Office(s) of the Paying Agent(s), the initial Specified Office of Principal Paying Agent being set out at the end of these Conditions.

(f) **Summaries:**

Certain provisions of these Conditions are summaries of the Trust Deed and the Agency Agreement and are subject to their detailed provisions. The holders of the Notes (the "**Noteholders**") and the holders of the related interest coupons, if any, (the "**Couponholders**" and the "**Coupons**", respectively) are entitled to the benefit of, are bound by, and are deemed to have notice of, all the provisions of the Trust Deed and the Agency Agreement applicable to them. Copies of the Trust Deed and the Agency Agreement are available for inspection by Noteholders during normal business hours at the Specified Office(s) of the Paying Agent(s).

2. Interpretation

(a) *Definitions:*

In these Conditions the following expressions have the following meanings:

"**Accrual Yield**" has the meaning given in the relevant Final Terms;

"**Additional Business Centre(s)**" means the city or cities specified as such in the relevant Final Terms;

"**Additional Financial Centre(s)**" means the city or cities specified as such in the relevant Final Terms;

"**Business Day**" means:

- (i) in relation to any sum payable in euro, a TARGET Settlement Day and a day on which commercial banks and foreign exchange markets settle payments generally in each (if any) Additional Business Centre; and
- (ii) in relation to any sum payable in a currency other than euro, a day on which commercial banks and foreign exchange markets settle payments generally in London, in the Principal Financial Centre of the relevant currency and in each (if any) Additional Business Centre;

"**Business Day Convention**", in relation to any particular date, has the meaning given in the relevant Final Terms and, if so specified in the relevant Final Terms, may have different meanings in relation to different dates and, in this context, the following expressions shall have the following meanings:

- (i) "**Following Business Day Convention**" means that the relevant date shall be postponed to the first following day that is a Business Day;
- (ii) "**Modified Following Business Day Convention**" or "**Modified Business Day Convention**" means that the relevant date shall be postponed to the first following day that is a Business Day unless that day falls in the next calendar month in which case that date will be the first preceding day that is a Business Day;
- (iii) "**Preceding Business Day Convention**" means that the relevant date shall be brought forward to the first preceding day that is a Business Day;
- (iv) "**FRN Convention**", "**Floating Rate Convention**" or "**Eurodollar Convention**" means that each relevant date shall be the date which numerically corresponds to the preceding such date in the calendar month which is the number of months specified in the relevant Final Terms as the Specified Period after the calendar month in which the preceding such date occurred, **provided, however, that:**
 - (A) if there is no such numerically corresponding day in the calendar month in which any such date should occur, then such date will be the last day which is a Business Day in that calendar month;
 - (B) if any such date would otherwise fall on a day which is not a Business Day, then such date will be the first following day which is a Business Day unless that day falls in the next calendar month, in which case it will be the first preceding day which is a Business Day; and
 - (C) if the preceding such date occurred on the last day in a calendar month which was a Business Day, then all subsequent such dates will be the last day which is a Business Day in the calendar month which is the specified number of months after the calendar month in which the preceding such date occurred; and

- (v) "**No Adjustment**" means that the relevant date shall not be adjusted in accordance with any Business Day Convention;

"**Calculation Agent**" means the Principal Paying Agent or such other Person specified in the relevant Final Terms as the party responsible for calculating the Rate(s) of Interest and Interest Amount(s) and/or such other amount(s) as may be specified in the relevant Final Terms;

"**Calculation Amount**" has the meaning given in the relevant Final Terms;

"**Consolidated Net Tangible Assets**" means the aggregate amount of consolidated total assets of the Issuer, after deducting therefrom (a) all liabilities due within one year (other than (x) short-term borrowings and (y) long-term debt due within one year) and (b) all goodwill, trade names, trademarks, patents and other like intangibles, as shown on the audited consolidated balance sheet contained in the last annual report to shareholders of the Issuer;

"**Coupon Sheet**" means, in respect of a Note, a coupon sheet relating to the Note;

"**Day Count Fraction**" means, in respect of the calculation of an amount for any period of time (the "**Calculation Period**"), such day count fraction as may be specified in these Conditions or the relevant Final Terms and:

- (i) if "**Actual/Actual (ICMA)**" is so specified, means:
- (a) where the Calculation Period is equal to or shorter than the Regular Period during which it falls, the actual number of days in the Calculation Period divided by the product of (1) the actual number of days in such Regular Period and (2) the number of Regular Periods in any year; and
 - (b) where the Calculation Period is longer than one Regular Period, the sum of:
 - (A) the actual number of days in such Calculation Period falling in the Regular Period in which it begins divided by the product of (1) the actual number of days in such Regular Period and (2) the number of Regular Periods in any year; and
 - (B) the actual number of days in such Calculation Period falling in the next Regular Period divided by the product of (a) the actual number of days in such Regular Period and (2) the number of Regular Periods in any year;
- (ii) if "**Actual/Actual (ISDA)**" is so specified, means the actual number of days in the Calculation Period divided by 365 (or, if any portion of the Calculation Period falls in a leap year, the sum of (A) the actual number of days in that portion of the Calculation Period falling in a leap year divided by 366 and (B) the actual number of days in that portion of the Calculation Period falling in a non-leap year divided by 365);
- (iii) if "**Actual/365 (Fixed)**" is so specified, means the actual number of days in the Calculation Period divided by 365;
- (iv) if "**Actual/360**" is so specified, means the actual number of days in the Calculation Period divided by 360;
- (v) if "**30/360**" is so specified, the number of days in the Calculation Period divided by 360, calculated on a formula basis as follows:

$$\text{Day Count Fraction} = \frac{[360 \times (Y_2 - Y_1)] + [30 \times (M_2 - M_1)] + (D_2 - D_1)}{360}$$

where:

"**Y₁**" is the year, expressed as a number, in which the first day of the Calculation Period falls;

"**Y₂**" is the year, expressed as a number, in which the day immediately following the last day included in the Calculation Period falls;

"**M₁**" is the calendar month, expressed as a number, in which the first day of the Calculation Period falls;

"**M₂**" is the calendar month, expressed as number, in which the day immediately following the last day included in the Calculation Period falls;

"**D₁**" is the first calendar day, expressed as a number, of the Calculation Period, unless such number would be 31, in which case **D₁** will be 30; and

"**D₂**" is the calendar day, expressed as a number, immediately following the last day included in the Calculation Period, unless such number would be 31 and **D₁** is greater than 29, in which case **D₂** will be 30";

- (vi) if "**30E/360**" or "**Eurobond Basis**" is so specified, the number of days in the Calculation Period divided by 360, calculated on a formula basis as follows:

$$\text{Day Count Fraction} = \frac{[360 \times (Y_2 - Y_1)] + [30 \times (M_2 - M_1)] + (D_2 - D_1)}{360}$$

where:

"**Y₁**" is the year, expressed as a number, in which the first day of the Calculation Period falls;

"**Y₂**" is the year, expressed as a number, in which the day immediately following the last day included in the Calculation Period falls;

"**M₁**" is the calendar month, expressed as a number, in which the first day of the Calculation Period falls;

"**M₂**" is the calendar month, expressed as a number, in which the day immediately following the last day included in the Calculation Period falls;

"**D₁**" is the first calendar day, expressed as a number, of the Calculation Period, unless such number would be 31, in which case **D₁** will be 30; and

"**D₂**" is the calendar day, expressed as a number, immediately following the last day included in the Calculation Period, unless such number would be 31, in which case **D₂** will be 30; and

- (vii) if "**30E/360 (ISDA)**" is so specified, the number of days in the Calculation Period divided by 360, calculated on a formula basis as follows:

$$\text{Day Count Fraction} = \frac{[360 \times (Y_2 - Y_1)] + [30 \times (M_2 - M_1)] + (D_2 - D_1)}{360}$$

where:

"**Y₁**" is the year, expressed as a number, in which the first day of the Calculation Period falls;

"**Y₂**" is the year, expressed as a number, in which the day immediately following the last day included in the Calculation Period falls;

"**M₁**" is the calendar month, expressed as a number, in which the first day of the Calculation Period falls;

"**M₂**" is the calendar month, expressed as a number, in which the day immediately following the last day included in the Calculation Period falls;

"**D₁**" is the first calendar day, expressed as a number, of the Calculation Period, unless (i) that day is the last day of February or (ii) such number would be 31, in which case D₁ will be 30; and

"**D₂**" is the calendar day, expressed as a number, immediately following the last day included in the Calculation Period, unless (i) that day is the last day of February but not the Maturity Date or (ii) such number would be 31, in which case D₂ will be 30,

provided, however, that in each such case the number of days in the Calculation Period is calculated from and including the first day of the Calculation Period to but excluding the last day of the Calculation Period;

"**Early Redemption Amount (Tax)**" means, in respect of any Note, its principal amount or such other amount as may be specified in, or determined in accordance with, the relevant Final Terms;

"**Early Termination Amount**" means, in respect of any Note, its principal amount or such other amount as may be specified in, or determined in accordance with, these Conditions or the relevant Final Terms;

"**EURIBOR**" means, in respect of any specified currency and any specified period, the interest rate benchmark known as the Euro zone interbank offered rate which is calculated and published by a designated distributor (currently Thomson Reuters) in accordance with the requirements from time to time of the European Banking Federation based on estimated interbank borrowing rates for a number of designated currencies and maturities which are provided, in respect of each such currency, by a panel of contributor banks (details of historic EURIBOR rates can be obtained from the designated distributor);

"**Extraordinary Resolution**" has the meaning given in the Trust Deed;

"**Final Redemption Amount**" means, in respect of any Note, its principal amount or such other amount as may be specified in, or determined in accordance with, the relevant Final Terms;

"**First Interest Payment Date**" means the date specified in the relevant Final Terms;

"**Fixed Coupon Amount**" has the meaning given in the relevant Final Terms;

"**Indebtedness**" means any indebtedness (whether being principal, premium, interest or other amounts) for or in respect of any notes, bonds, debentures, debenture stock, loan stock or other securities or any borrowed money or any liability under or in respect of any acceptance or acceptance credit;

"**Interest Amount**" means, in relation to a Note and an Interest Period, the amount of interest payable in respect of that Note for that Interest Period;

"**Interest Commencement Date**" means the Issue Date of the Notes or such other date as may be specified as the Interest Commencement Date in the relevant Final Terms;

"**Interest Determination Date**" has the meaning given in the relevant Final Terms;

"Interest Payment Date" means the First Interest Payment Date and any date or dates specified as such in, or determined in accordance with the provisions of, the relevant Final Terms and, if a Business Day Convention is specified in the relevant Final Terms:

- (i) as the same may be adjusted in accordance with the relevant Business Day Convention; or
- (ii) if the Business Day Convention is the FRN Convention, Floating Rate Convention or Eurodollar Convention and an interval of a number of calendar months is specified in the relevant Final Terms as being the Specified Period, each of such dates as may occur in accordance with the FRN Convention, Floating Rate Convention or Eurodollar Convention at such Specified Period of calendar months following the Interest Commencement Date (in the case of the first Interest Payment Date) or the previous Interest Payment Date (in any other case);

"Interest Period" means each period beginning on (and including) the Interest Commencement Date or any Interest Payment Date and ending on (but excluding) the next Interest Payment Date;

"ISDA Benchmarks Supplement" means the ISDA Benchmarks Supplement (as amended and updated as at the date of issue of the first Tranche of the Notes of the relevant Series (as specified in the relevant Pricing Supplement)) published by the International Swaps and Derivatives Association, Inc;

"ISDA Definitions" means the 2006 ISDA Definitions (as amended and updated as at the date of issue of the first Tranche of the Notes of the relevant Series (as specified in the relevant Final Terms) as published by the International Swaps and Derivatives Association, Inc.);

"Issue Date" has the meaning given in the relevant Final Terms;

"LIBOR" means the interest rate benchmark known as the London interbank offered rate administered by the ICE Benchmark Administration (or any other person which takes over the administration of that rate) for the relevant currency and period displayed on pages LIBOR01 or LIBOR02 of the Reuters screen (or any replacement Reuters page which displays that rate) on the appropriate page of such other information service which publishes that rate from time to time in place of Reuters (details of historic LIBOR rates can be obtained from Reuters or the designated information service from time to time);

"Margin" has the meaning given in the relevant Final Terms;

"Maturity Date" has the meaning given in the relevant Final Terms;

"Maximum Redemption Amount" has the meaning given in the relevant Final Terms;

"Minimum Redemption Amount" has the meaning given in the relevant Final Terms;

"Optional Redemption Amount (Call)" means, in respect of any Note, its principal amount or such other amount as may be specified in, or determined in accordance with, the relevant Final Terms;

"Optional Redemption Amount (Put)" means, in respect of any Note, its principal amount or such other amount as may be specified in, or determined in accordance with, the relevant Final Terms;

"Optional Redemption Date (Call)" has the meaning given in the relevant Final Terms;

"Optional Redemption Date (Put)" has the meaning given in the relevant Final Terms;

"Participating Member State" means a Member State of the European Communities which adopts the euro as its lawful currency in accordance with the Treaty;

"Par Redemption Date" has the meaning given in the relevant Final Terms;

"Paying Agents" means the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent and any substitute or additional paying agents appointed in accordance with the Agency Agreement and a **"Paying Agent"** means any of them;

"Payment Business Day" means:

- (i) if the currency of payment is euro, any day which is:
 - (A) a day on which banks in the relevant place of presentation are open for presentation and payment of bearer debt securities and for dealings in foreign currencies; and
 - (B) in the case of payment by transfer to an account, a TARGET Settlement Day and a day on which dealings in foreign currencies may be carried on in each (if any) Additional Financial Centre; or
- (ii) if the currency of payment is not euro, any day which is:
 - (A) a day on which banks in the relevant place of presentation are open for presentation and payment of bearer debt securities and for dealings in foreign currencies; and
 - (B) in the case of payment by transfer to an account, a day on which dealings in foreign currencies may be carried on in the Principal Financial Centre of the currency of payment and in each (if any) Additional Financial Centre;

"Permitted Security Interest" means:

- (i) any Security Interest over Relevant Assets and the shares of stock or Indebtedness of the Issuer and its Restricted Subsidiaries securing Indebtedness of the Issuer and its Restricted Subsidiaries the principal amount of which (when aggregated with the principal amount of any other Indebtedness which has the benefit of any Security Interest over Relevant Assets and the shares of stock or Indebtedness of the Issuer and its Restricted Subsidiaries) does not at the time exceed 15 per cent. of the Consolidated Net Tangible Assets;
- (ii) any Security Interest on property, shares of stock or Indebtedness of any Person existing at the time such Person becomes a Restricted Subsidiary;
- (iii) any Security Interest on property or shares of stock existing at the time of acquisition of that property or those shares of stock, or to secure the payment of all or any part of the purchase price of that property or those shares of stock, or to secure any debt incurred before, at the time of, or within twelve months after, in the case of shares of stock, the acquisition of such shares of stock and, in the case of property, the later of the acquisition, completion of construction (including any improvements on an existing property) or commencement of the commercial operation of the property, where the debt is incurred to finance all or any part of the purchase price thereof;
- (iv) any Security Interest securing Indebtedness owed to the Issuer or to any of its Restricted Subsidiaries by the Issuer or any of its Restricted Subsidiaries;
- (v) any Security Interest existing at the Issue Date of the Notes;
- (vi) any Security Interest on a Relevant Asset to secure Indebtedness incurred to finance all or part of the cost of improving, constructing, altering or repairing any building, equipment or facilities or of any other improvements on all or any part of that Relevant Asset, if such Indebtedness is incurred before, during, or within twelve months after completing the improvement, construction, alteration or repair;
- (vii) any Security Interest on property owned or held by any Person or on shares of stock or Indebtedness of any Person, where the Security Interest existed either at the time the corporation is merged, consolidated or amalgamated with either the Issuer or a

- Restricted Subsidiary or at the time of a sale, lease or other disposition of all or substantially all of the property of a Person to the Issuer or a Restricted Subsidiary;
- (viii) any Security Interest arising by operation of law and not securing amounts more than 90 days overdue or otherwise being contested in good faith;
 - (ix) any Security Interest arising by operation of law over any credit balance or cash held in any account with a financial institution;
 - (x) any rights of financial institutions to offset credit balances in connection with the operation of cash management programs established for the benefit of the Issuer and/or the benefit of any Restricted Subsidiary;
 - (xi) any Security Interest incurred or deposits made in the ordinary course of business, including but not limited to:
 - (a) any mechanics', materialmen's, carriers', workmen's, vendors' or other similar Security Interests;
 - (b) any Security Interests securing amounts in connection with workers' compensation, unemployment insurance and other types of social security; or
 - (c) any easements, rights-of-way, restrictions and other similar charges;
 - (xii) any Security Interest incurred or deposit made securing the performance of tenders, bids, leases, statutory obligations, surety and appeal bonds, government contracts, performance and return of money bonds and other obligations of a similar nature incurred in the ordinary course of business;
 - (xiii) any Security Interest securing taxes or assessments or other applicable governmental charges or levies;
 - (xiv) any extension, renewal or replacement or successive extensions, renewals or replacements, in whole or in part, of any Security Interest described in paragraphs (a) to (m) above or of any Indebtedness secured by a Security Interest described in paragraphs (a) to (m) above, so long as the principal amount of Indebtedness secured does not exceed the principal amount of Indebtedness secured at the time of the extension, renewal or replacement, and that the extension, renewal or replacement Security Interest is limited to all or any part of the same property or shares of stock that secured the Security Interest extended, renewed or replaced (including improvements on that property), or property received or shares of stock issued in substitution or exchange;
 - (xv) any Security Interest in favour of the Issuer or any of its Subsidiaries; and
 - (xvi) any Security Interest on property of the Issuer or a Restricted Subsidiary in favour of the United States or any State of the United States, or the United Kingdom, or any other country, or any political subdivision of, or any department, agency or instrumentality of, these countries or states, to secure partial, progress, advance or other payments under provisions of any contract or statute including, but not limited to, Security Interests to secure Indebtedness of pollution control or industrial revenue bond type, or to secure any Indebtedness incurred for the purpose of financing all or any part of the purchase price or cost of construction of the property subject to these Security Interests;

"Person" means any individual, company, corporation, firm, partnership, joint venture, association, organisation, state or agency of a state or other entity, whether or not having separate legal personality;

"Principal Financial Centre" means, in relation to any currency, the principal financial centre for that currency, **provided, however, that:**

- (i) in relation to euro, it means the principal financial centre of such Member State of the European Communities as is selected (in the case of a payment) by the payee or (in the case of a calculation) by the Calculation Agent; and
- (ii) in relation to Australian dollars, it means either Sydney or Melbourne and, in relation to New Zealand dollars, it means either Wellington or Auckland; in each case as is selected (in the case of a payment) by the payee or (in the case of a calculation) by the Calculation Agent;

"Put Option Notice" means a notice which must be delivered to a Paying Agent by any Noteholder wanting to exercise a right to redeem a Note at the option of the Noteholder pursuant to Condition 9(f) (*Redemption at the option of Noteholders*);

"Put Option Receipt" means a receipt issued by a Paying Agent to a depositing Noteholder upon deposit of a Note with such Paying Agent by any Noteholder wanting to exercise a right to redeem a Note at the option of the Noteholder;

"Rate of Interest" means the rate or rates (expressed as a percentage per annum) of interest payable in respect of the Notes specified in the relevant Final Terms or calculated or determined in accordance with the provisions of these Conditions and/or the relevant Final Terms;

"Redemption Amount" means, as appropriate, the Final Redemption Amount, the Early Redemption Amount (Tax), the Optional Redemption Amount (Call), the Optional Redemption Amount (Put), the Early Termination Amount or such other amount in the nature of a redemption amount as may be specified in, or determined in accordance with the provisions of, the relevant Final Terms;

"Reference Banks" has the meaning given in the relevant Final Terms or, if none, four major banks selected by the Issuer or an agent appointed at the time in the market that is most closely connected with the Reference Rate;

"Reference Price" has the meaning given in the relevant Final Terms;

"Reference Rate" has the meaning given in the relevant Final Terms;

"Regular Period" means:

- (i) in the case of Notes where interest is scheduled to be paid only by means of regular payments, each period from and including the Interest Commencement Date to but excluding the first Interest Payment Date and each successive period from and including one Interest Payment Date to but excluding the next Interest Payment Date;
- (ii) in the case of Notes where, apart from the first Interest Period, interest is scheduled to be paid only by means of regular payments, each period from and including a Regular Date falling in any year to but excluding the next Regular Date, where **"Regular Date"** means the day and month (but not the year) on which any Interest Payment Date falls; and
- (iii) in the case of Notes where, apart from one Interest Period other than the first Interest Period, interest is scheduled to be paid only by means of regular payments, each period from and including a Regular Date falling in any year to but excluding the next Regular Date, where **"Regular Date"** means the day and month (but not the year) on which any Interest Payment Date falls other than the Interest Payment Date falling at the end of the irregular Interest Period;

"Relevant Asset" means any manufacturing plant or facility or any research facility owned by the Issuer or any of its Restricted Subsidiaries which is located within the United States or the United Kingdom and having a gross book value (before deducting any depreciation

reserve), as of the date of determination, exceeding 2 per cent. of the Issuer's Consolidated Net Tangible Assets other than:

- (i) any plant or facility or research facility which, in the opinion of the board of directors of the Issuer, is not materially important to the total business conducted by the Issuer and its subsidiaries considered as a whole; or
- (ii) any portion of a property described above which, in the opinion of the board of directors of the Issuer, is not materially important to the use or operation of such property;

"Relevant Date" means, in relation to any payment, whichever is the later of (a) the date on which the payment in question first becomes due and (b) if the full amount payable has not been received in the Principal Financial Centre of the currency of payment by the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent on or prior to such due date, the date on which (the full amount having been so received) notice to that effect has been given to the Noteholders;

"Relevant Financial Centre" has the meaning given in the relevant Final Terms;

"Relevant Screen Page" means the page, section or other part of a particular information service (including, without limitation, Reuters) specified as the Relevant Screen Page in the relevant Final Terms, or such other page, section or other part as may replace it on that information service or such other information service, in each case, as may be nominated by the Person providing or sponsoring the information appearing there for the purpose of displaying rates or prices comparable to the Reference Rate;

"Relevant Time" has the meaning given in the relevant Final Terms;

"Reserved Matter" means any proposal:

- (i) to change any date fixed for payment of principal or interest in respect of the Notes, to reduce the amount of principal or interest payable on any date in respect of the Notes or to alter the method of calculating the amount of any payment in respect of the Notes on redemption or maturity;
- (ii) to effect the exchange or substitution of the Notes for, or the conversion of the Notes into, shares, bonds or other obligations or securities of the Issuer or any other person or body corporate formed or to be formed (other than as permitted under Clause 7.3 of the Trust Deed);
- (iii) to change the currency in which amounts due in respect of the Notes are payable;
- (iv) to change the quorum required at any meeting of Noteholders or the majority required to pass an Extraordinary Resolution; or
- (v) to amend this definition;

"Restricted Subsidiary" means any Wholly-Owned Subsidiary of the Issuer other than a Wholly-Owned Subsidiary principally engaged in leasing or financing instalment receivables or principally engaged in financing the operations of the Issuer and its consolidated subsidiaries:

- (i) with substantially all of its property located within the United Kingdom or the United States; and
- (ii) which owns a Relevant Asset;

"Security Interest" means any mortgage, charge, pledge, lien or other security interest including, without limitation, anything analogous to any of the foregoing under the laws of any jurisdiction;

"**Specified Currency**" has the meaning given in the relevant Final Terms;

"**Specified Denomination(s)**" has the meaning given in the relevant Final Terms;

"**Specified Office**" has the meaning given in the Agency Agreement;

"**Specified Period**" has the meaning given in the relevant Final Terms;

"**Subsidiary**" means, in relation to any Person (the "**first Person**") at any particular time, any other Person (the "**second Person**"):

- (i) whose affairs and policies the first Person controls or has the power to control, whether by ownership of share capital, contract, the power to appoint or remove members of the governing body of the second Person or otherwise; or
- (ii) whose financial statements are, in accordance with applicable law and generally accepted accounting principles, consolidated with those of the first Person;

"**Talon**" means a talon for further Coupons;

"**TARGET2**" means the Trans-European Automated Real-Time Gross Settlement Express Transfer payment system which utilises a single shared platform and which was launched on 19 November 2007;

"**TARGET Settlement Day**" means any day on which TARGET2 is open for the settlement of payments in euro;

"**Treaty**" means the Treaty establishing the European Communities, as amended;

"**Wholly-Owned Subsidiary**" means any Person in which the Issuer, and/or one or more of its Wholly-Owned Subsidiaries, controls, directly or indirectly, all of the stock with ordinary voting power to elect the board of directors of that Person; and

"**Zero Coupon Note**" means a Note specified as such in the relevant Final Terms.

(b) **Interpretation:**

In these Conditions:

- (i) if the Notes are Zero Coupon Notes, references to Coupons and Couponholders are not applicable;
- (ii) if Talons are specified in the relevant Final Terms as being attached to the Notes at the time of issue, references to Coupons shall be deemed to include references to Talons;
- (iii) if Talons are not specified in the relevant Final Terms as being attached to the Notes at the time of issue, references to Talons are not applicable;
- (iv) any reference to principal shall be deemed to include the Redemption Amount, any additional amounts in respect of principal which may be payable under Condition 11 (*Taxation*), any premium payable in respect of a Note and any other amount in the nature of principal payable pursuant to these Conditions;
- (v) any reference to interest shall be deemed to include any additional amounts in respect of interest which may be payable under Condition 11 (*Taxation*) and any other amount in the nature of interest payable pursuant to these Conditions;
- (vi) references to Notes being "outstanding" shall be construed in accordance with the Trust Deed;
- (vii) if an expression is stated in Condition 2(a) (*Definitions*) to have the meaning given in the relevant Final Terms, but the relevant Final Terms gives no such meaning or

specifies that such expression is "not applicable" then such expression is not applicable to the Notes; and

- (viii) any reference to the Agency Agreement or the Trust Deed shall be construed as a reference to the Agency Agreement or the Trust Deed, as the case may be, as amended and/or supplemented up to and including the Issue Date of the Notes.

3. **Form, Denomination and Title**

The Notes are in bearer form in the Specified Denomination(s) with Coupons and, if specified in the relevant Final Terms, Talons attached at the time of issue. In the case of a Series of Notes with more than one Specified Denomination, Notes of one Specified Denomination will not be exchangeable for Notes of another Specified Denomination. Title to the Notes and the Coupons will pass by delivery. The holder of any Note or Coupon shall (except as otherwise required by law) be treated as its absolute owner for all purposes (whether or not it is overdue and regardless of any notice of ownership, trust or any other interest therein, any writing thereon or any notice of any previous loss or theft thereof) and no Person shall be liable for so treating such holder. No person shall have any right to enforce any term or condition of any Note or the Trust Deed under the Contracts (Rights of Third Parties) Act 1999.

4. **Status**

The Notes constitute direct, general and unconditional obligations of the Issuer which will at all times rank *pari passu* among themselves and at least *pari passu* with all other present and future unsecured obligations of the Issuer, save for such obligations as may be preferred by provisions of law that are both mandatory and of general application.

5. **Negative Pledge**

So long as any Note remains outstanding, the Issuer shall not, and shall procure that none of its Restricted Subsidiaries will, create or permit to subsist any Security Interest other than a Permitted Security Interest over any Relevant Asset or any shares of stock or Indebtedness of any Restricted Subsidiary without at the same time or prior thereto securing the Notes equally and rateably therewith.

6. **Fixed Rate Note Provisions**

(a) ***Application:***

This Condition 6 is applicable to the Notes only if the Fixed Rate Note provisions are specified in the relevant Final Terms as being applicable.

(b) ***Accrual of interest:***

The Notes bear interest from the Interest Commencement Date at the Rate of Interest payable in arrear on each Interest Payment Date, subject as provided in Condition 10 (*Payments*). Each Note will cease to bear interest from the due date for final redemption unless, upon due presentation, payment of the Redemption Amount is improperly withheld or refused, in which case it will continue to bear interest in accordance with this Condition 6 (as well after as before judgment) until whichever is the earlier of (i) the day on which all sums due in respect of such Note up to that day are received by or on behalf of the relevant Noteholder and (ii) the day which is seven days after the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent has notified the Noteholders that it has received all sums due in respect of the Notes up to such seventh day (except to the extent that there is any subsequent default in payment).

(c) ***Fixed Coupon Amount:***

The amount of interest payable in respect of each Note for any Interest Period shall be the relevant Fixed Coupon Amount and, if the Notes are in more than one Specified Denomination, shall be the relevant Fixed Coupon Amount in respect of the relevant Specified Denomination.

(d) ***Calculation of interest amount:***

The amount of interest payable in respect of each Note for any period for which a Fixed Coupon Amount is not specified shall be calculated by applying the Rate of Interest to the Calculation Amount, multiplying the product by the relevant Day Count Fraction, rounding the resulting figure to the nearest sub-unit of the Specified Currency (half a sub-unit being rounded upwards) and multiplying such rounded figure by a fraction equal to the Specified Denomination of such Note divided by the Calculation Amount. For this purpose a "**sub-unit**" means, in the case of any currency other than euro, the lowest amount of such currency that is available as legal tender in the country of such currency and, in the case of euro, means one cent.

7. **Floating Rate Note Provisions**

(a) ***Application:***

This Condition 7 is applicable to the Notes only if the Floating Rate Note provisions are specified in the relevant Final Terms as being applicable.

(b) ***Accrual of interest:***

The Notes bear interest from the Interest Commencement Date at the Rate of Interest payable in arrear on each Interest Payment Date, subject as provided in Condition 10 (*Payments*). Each Note will cease to bear interest from the due date for final redemption unless, upon due presentation, payment of the Redemption Amount is improperly withheld or refused, in which case it will continue to bear interest in accordance with this Condition 7 (as well after as before judgment) until whichever is the earlier of (i) the day on which all sums due in respect of such Note up to that day are received by or on behalf of the relevant Noteholder and (ii) the day which is seven days after the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent has notified the Noteholders that it has received all sums due in respect of the Notes up to such seventh day (except to the extent that there is any subsequent default in payment).

(c) ***Screen Rate Determination:***

If Screen Rate Determination is specified in the relevant Final Terms as the manner in which the Rate(s) of Interest is/are to be determined, the Rate of Interest applicable to the Notes for each Interest Period will be determined by the Calculation Agent on the following basis:

- (i) if the Reference Rate is a composite quotation or customarily supplied by one entity, the Calculation Agent will determine the Reference Rate which appears on the Relevant Screen Page as of the Relevant Time on the relevant Interest Determination Date;
- (ii) in any other case, the Calculation Agent will determine the arithmetic mean of the Reference Rates which appear on the Relevant Screen Page as of the Relevant Time on the relevant Interest Determination Date;
- (iii) if, in the case of (i) above, such rate does not appear on that page or, in the case of (ii) above, fewer than two such rates appear on that page or if, in either case, the Relevant Screen Page is unavailable, the Calculation Agent will:
 - (A) request the principal Relevant Financial Centre office of each of the Reference Banks to provide a quotation of the Reference Rate at approximately the Relevant Time on the Interest Determination Date to prime banks in the Relevant Financial Centre interbank market in an amount that is representative for a single transaction in that market at that time; and
 - (B) determine the arithmetic mean of such quotations; and
- (iv) if fewer than two such quotations are provided as requested, the Calculation Agent will determine the arithmetic mean of the rates (being the nearest to the Reference

Rate, as determined by the Calculation Agent) quoted by major banks in the Principal Financial Centre of the Specified Currency, selected by the Calculation Agent, at approximately 11.00 a.m. (local time in the Principal Financial Centre of the Specified Currency) on the first day of the relevant Interest Period for loans in the Specified Currency to leading European banks for a period equal to the relevant Interest Period and in an amount that is representative for a single transaction in that market at that time,

and the Rate of Interest for such Interest Period shall be the sum of the Margin and the rate or (as the case may be) the arithmetic mean so determined; **provided, however, that** if the Calculation Agent is unable to determine a rate or (as the case may be) an arithmetic mean in accordance with the above provisions in relation to any Interest Period, the Rate of Interest applicable to the Notes during such Interest Period will be the sum of the Margin and the rate or (as the case may be) the arithmetic mean last determined in relation to the Notes in respect of a preceding Interest Period.

(d) ***ISDA Determination:***

If ISDA Determination is specified in the relevant Final Terms as the manner in which the Rate(s) of Interest is/are to be determined, the Rate of Interest applicable to the Notes for each Interest Period will be the sum of the Margin and the relevant ISDA Rate where "**ISDA Rate**" in relation to any Interest Period means a rate equal to the Floating Rate (as defined in the ISDA Definitions) that would be determined by the Calculation Agent under an interest rate swap transaction if the Calculation Agent were acting as Calculation Agent for that interest rate swap transaction under the terms of an agreement incorporating the ISDA Definitions and under which:

- (i) the Floating Rate Option (as defined in the ISDA Definitions) is as specified in the relevant Final Terms;
- (ii) the Designated Maturity (as defined in the ISDA Definitions) is a period specified in the relevant Final Terms; and
- (iii) the relevant Reset Date (as defined in the ISDA Definitions) is either (A) if the relevant Floating Rate Option is based on the London inter-bank offered rate (LIBOR) for a currency, the first day of that Interest Period or (B) in any other case, as specified in the relevant Final Terms.

(e) ***Maximum or Minimum Rate of Interest***

If any Maximum Rate of Interest or Minimum Rate of Interest is specified in the relevant Final Terms, then the Rate of Interest shall in no event be greater than the maximum or be less than the minimum so specified.

(f) ***Calculation of Interest Amount:***

The Calculation Agent will, as soon as practicable after the time at which the Rate of Interest is to be determined in relation to each Interest Period, calculate the Interest Amount payable in respect of each Note for such Interest Period. The Interest Amount will be calculated by applying the Rate of Interest for such Interest Period to the Calculation Amount, multiplying the product by the relevant Day Count Fraction, rounding the resulting figure to the nearest sub-unit of the Specified Currency (half a sub-unit being rounded upwards) and multiplying such rounded figure by a fraction equal to the Specified Denomination of the relevant Note divided by the Calculation Amount. For this purpose a "**sub-unit**" means, in the case of any currency other than euro, the lowest amount of such currency that is available as legal tender in the country of such currency and, in the case of euro, means one cent.

(g) ***Calculation of other amounts:***

If the relevant Final Terms specifies that any other amount is to be calculated by the Calculation Agent, the Calculation Agent will, as soon as practicable after the time or times at which any such amount is to be determined, calculate the relevant amount. The relevant

amount will be calculated by the Calculation Agent in the manner specified in the relevant Final Terms.

(h) ***Publication:***

The Calculation Agent will cause each Rate of Interest and Interest Amount determined by it, together with the relevant Interest Payment Date, and any other amount(s) required to be determined by it together with any relevant payment date(s) to be notified to the Paying Agents and each competent authority, stock exchange and/or quotation system (if any) by which the Notes have then been admitted to listing, trading and/or quotation as soon as practicable after such determination but (in the case of each Rate of Interest, Interest Amount and Interest Payment Date) in any event not later than the first day of the relevant Interest Period. Notice thereof shall also promptly be given to the Noteholders. The Calculation Agent will be entitled to recalculate any Interest Amount (on the basis of the foregoing provisions) without notice in the event of an extension or shortening of the relevant Interest Period. If the Calculation Amount is less than the minimum Specified Denomination the Calculation Agent shall not be obliged to publish each Interest Amount but instead may publish only the Calculation Amount and the Interest Amount in respect of a Note having the minimum Specified Denomination.

(i) ***Benchmark Discontinuation***

- (i) If a Benchmark Event occurs in relation to the Reference Rate when the Rate of Interest (or any component part thereof) for any Interest Period remains to be determined by reference to such Reference Rate, then the Issuer shall use its reasonable endeavours to select and appoint an Independent Adviser, as soon as reasonably practicable, to determine a Successor Rate, failing which an Alternative Rate (in accordance with Condition 7(i)(ii)) and, in either case, an Adjustment Spread, if any (in accordance with Condition 7(i)(iii)) and any Benchmark Amendments (in accordance with Condition 7(i)(iv)).

In the absence of bad faith or fraud, the Independent Adviser shall have no liability whatsoever to the Issuer, the Trustee, the Paying Agents or the Noteholders for any determination made by it pursuant to this Condition 7(i).

If (i) the Issuer is unable to select and appoint an Independent Adviser or (ii) the Independent Adviser selected and appointed by it fails to determine a Successor Rate or, failing which, an Alternative Rate in accordance with this Condition 7(i) prior to the relevant Interest Determination Date, the Reference Rate applicable to the immediate following Interest Period shall be the Reference Rate applicable as at the last preceding Interest Determination Date. If there has not been a first Interest Payment Date, the Reference Rate shall be the Reference Rate applicable to the first Floating Rate Interest Period. For the avoidance of doubt, any adjustment pursuant to this final paragraph of Condition 7(i) shall apply to the immediately following Interest Period only. Any subsequent Interest Period may be subject to the subsequent operation of this Condition 7(i).

- (ii) If the Independent Adviser determines in its discretion that:

- (A) there is a Successor Rate, then such Successor Rate shall (subject to adjustment as provided in Condition 7(i)(iii)) subsequently be used in place of the Reference Rate to determine the Rate of Interest for the immediately following Interest Period and all following Interest Periods, subject to the subsequent operation of this Condition 7(i); or
- (B) there is no Successor Rate but that there is an Alternative Rate, then such Alternative Rate shall (subject to adjustment as provided in Condition 7(i)(iii)) subsequently be used in place of the Reference Rate to determine the Rate of Interest for the immediately following Interest Period and all following Interest Periods, subject to the subsequent operation of this Condition 7(i).

- (iii) If the Independent Adviser determines in its discretion (A) that an Adjustment Spread is required to be applied to the Successor Rate or the Alternative Rate (as the case may be) and (B) the quantum of, or a formula or methodology for determining, such Adjustment Spread, then such Adjustment Spread shall apply to the Successor Rate or the Alternative Rate (as the case may be).
- (iv) If any relevant Successor Rate, Alternative Rate or Adjustment Spread is determined in accordance with this Condition 7(i) and the Independent Adviser determines in its discretion (A) that amendments to these Conditions, the Trust Deed or the Agency Agreement are necessary to ensure the proper operation of such Successor Rate, Alternative Rate and/or Adjustment Spread (such amendments, the "**Benchmark Amendments**") and (B) the terms of the Benchmark Amendments, then the Issuer shall, subject to giving notice thereof in accordance with Condition 7(i)(vi), without any requirement for the consent or approval of relevant Noteholders or Couponholders, vary or amend these Conditions, the Trust Deed and the Agency Agreement to give effect to such Benchmark Amendments with effect from the date specified in such notice.
- (v) The Trustee shall, at the request and expense of the Issuer and without the requirement for any consent or approval of the Noteholders or Couponholders, concur with the Issuer in effecting any Benchmark Amendments as may be required in order to give effect to this Condition 7(i) (which, for the avoidance of doubt, shall not be treated as being within the scope of the Reserved Matters (as defined in the Trust Deed)), subject to receipt by the Trustee of the certificate referred to in subparagraph (vii) below, *provided however*, that the Trustee shall not be obliged so to concur if in the reasonable opinion of the Trustee, doing so would have the effect of imposing more onerous obligations upon it or expose it to any additional duties, responsibilities or liabilities or reduce or amend the protective provisions in these Conditions, the Agency Agreement or the Trust Deed (including, for the avoidance of doubt, any documents supplemental thereto). For the avoidance of doubt, none of the Trustee, the Paying Agents or the Calculation Agent will be responsible for determining whether or not a Benchmark Event has occurred.
- (vi) Any Successor Rate, Alternative Rate, Adjustment Spread and the specific terms of any Benchmark Amendments, as determined under this Condition 7(i) will be notified promptly by the Issuer to the Trustee, the Paying Agents, the Calculation Agent and, in accordance with Condition 18 (*Notices*), the Noteholders. Such notice shall be irrevocable and shall specify the effective date of the Benchmark Amendments, if any.
- (vii) No later than notifying the Trustee of the same, the Issuer shall deliver to the Trustee a certificate signed by an authorised signatory of the Issuer:
 - (A) confirming (x) that a Benchmark Event has occurred, (y) the relevant Successor Rate, or, as the case may be, the relevant Alternative Rate and, (z) where applicable, any relevant Adjustment Spread and/or the specific terms of any relevant Benchmark Amendments, in each case as determined in accordance with the provisions of this Condition 7(i); and
 - (B) certifying that the relevant Benchmark Amendments are necessary to ensure the proper operation of such relevant Successor Rate, Alternative Rate and/or Adjustment Spread.

The Trustee shall be entitled to rely on such certificate (without further enquiry and without liability to any person) as sufficient evidence thereof.

- (viii) The Successor Rate or Alternative Rate and the Adjustment Spread (if any) and the Benchmark Amendments (if any) determined in accordance with this Condition 7(i) will (in the absence of manifest error, bad faith or fraud in the determination of the Successor Rate or Alternative Rate, and the Adjustment Spread (if any) and the

Benchmark Amendments (if any)), be binding on the Issuer, the Noteholders, the Trustee, the Paying Agents and the Calculation Agent.

(ix) Without prejudice to the obligations of the Issuer under Condition 7(i)(i), (ii), (iii) and (iv), the Reference Rate and the fallback provisions provided for in Condition 7(c) will continue to apply unless and until a Benchmark Event has occurred.

(x) As used in this Condition 7(i):

"Adjustment Spread" means either a spread (which may be positive or negative), or the formula or methodology for calculating a spread, in either case, which the Independent Adviser determines is required to be applied to the relevant Successor Rate or the relevant Alternative Rate (as the case may be) to reduce or eliminate, to the extent reasonably practicable in the circumstances, any economic prejudice or benefit (as the case may be) to Noteholders as a result of the replacement of the Reference Rate with the Successor Rate or the Alternative Rate (as the case may be) and is the spread, formula or methodology which:

(A) in the case of a Successor Rate, is formally recommended in relation to the replacement of the Reference Rate with the Successor Rate by any Relevant Nominating Body; or

(B) (if no such recommendation has been made, or in the case of an Alternative Rate) the Independent Adviser determines, is recognised or acknowledged as being the industry standard for over-the-counter derivative transactions which reference the Reference Rate, where such rate has been replaced by the Successor Rate or the Alternative Rate (as the case may be); or

(C) (if the Independent Adviser determines that no such industry standard is recognised or acknowledged) the Independent Adviser determines to be appropriate.

"Alternative Rate" means an alternative benchmark or screen rate which the Independent Adviser determines in accordance with Condition 7(i)(ii) is customary in market usage in the international debt capital markets for the purposes of determining floating rates of interest (or the relevant component part thereof) in the Specified Currency.

"Benchmark Amendments" has the meaning given to it in Condition 7(i)(iv).

"Benchmark Event" means:

(A) the Reference Rate ceasing to be published for a period of at least five (5) Business Days or ceasing to exist; or

(B) a public statement by the administrator of the Reference Rate that it will cease publishing the Reference Rate permanently or indefinitely (in circumstances where no successor administrator has been appointed that will continue publication of the Reference Rate); or

(C) a public statement by the supervisor of the administrator of the Reference Rate, that the Reference Rate has been or will permanently or indefinitely discontinued; or

(D) a public statement by the supervisor of the administrator of the Reference Rate as a consequence of which the Reference Rate will be prohibited from being used either generally, or in respect of the relevant Floating Rate Notes; or

(E) there has taken place (or will otherwise take place, prior to the next following Interest Determination Date) a change in customary market practice in the international debt capital markets applicable generally to floating rate notes

denominated in the Specified Currency (determined according to factors including, but not limited to, public statements, opinions and publications of industry bodies and organisations) to refer to a base rate other than the Reference Rate specified in the applicable Final Terms despite the continued existence of such Reference Rate, when any Rate of Interest (or any component part thereof) remains to be determined by reference to the Reference Rate; or

- (F) it has become unlawful for the Calculation Agent, the Issuer or any other party to calculate any Rate of Interest using the Reference Rate;

"Independent Adviser" means an independent financial institution of international repute or other independent financial adviser experienced in the international capital markets, in each case selected and appointed by the Issuer at its own expense under Condition 7(i)(i).

"Relevant Nominating Body" means, in respect of a benchmark or screen rate (as applicable):

- (A) the central bank for the currency to which the benchmark or screen rate (as applicable) relates, or any central bank or other supervisory authority which is responsible for supervising the administrator of the benchmark or screen rate (as applicable); or
- (B) any working group or committee sponsored by, chaired or co-chaired by or constituted at the request of (a) the central bank for the currency to which the benchmark or screen rate (as applicable) relates, (b) any central bank or other supervisory authority which is responsible for supervising the administrator of the benchmark or screen rate (as applicable), (c) a group of the aforementioned central banks or other supervisory authorities or (d) the Financial Stability Board or any part thereof.

"Successor Rate" means a successor to or replacement of the Reference Rate which is formally recommended by any Relevant Nominating Body.

(j) ***Notifications etc.:***

All notifications, opinions, determinations, certificates, calculations, quotations and decisions given, expressed, made or obtained for the purposes of this Condition 7 by the Calculation Agent will (in the absence of manifest error) be binding on the Issuer, the Trustee, the Paying Agents, the Noteholders and the Couponholders and (subject as aforesaid) no liability to any such Person will attach to the Calculation Agent in connection with the exercise or non-exercise by it of its powers, duties and discretions for such purposes.

(k) ***Determination or Calculation by Trustee:***

If the Calculation Agent fails at any time to determine a Rate of Interest or to calculate an Interest Amount, the Trustee will determine such Rate of Interest and make such determination or calculation which shall be deemed to have been made by the Calculation Agent. In doing so, the Trustee shall apply all of the provisions of these Conditions with any necessary consequential amendments to the extent that, in its sole opinion and with absolute discretion, it can do so and in all other respects it shall do so in such manner as it shall deem fair and reasonable in all the circumstances and will not be liable for any loss, liability, cost, charge or expense which may arise as a result thereof. Any such determination or calculation made by the Trustee shall be binding on the Issuer, the Noteholders and the Couponholders.

(l) ***Calculation Agent***

Notwithstanding any other provision of this Condition 7, if in the Calculation Agent's opinion there is any uncertainty between two or more alternative courses of action in making any determination or calculation under this Condition 7, the Calculation Agent shall promptly notify the Issuer and the Independent Adviser thereof and the Issuer and the Independent

Adviser shall direct the Calculation Agent in writing as to which alternative course of action to adopt. If the Calculation Agent is not promptly provided with such direction, or is otherwise unable to make such calculation or determination for any reason, it shall notify the Issuer and the Independent Adviser thereof and the Calculation Agent shall be under no obligation to make such calculation or determination and shall not incur any liability for not doing so.

8. **Zero Coupon Note Provisions**

(a) ***Application:***

This Condition 8 is applicable to the Notes only if the Zero Coupon Note provisions are specified in the relevant Final Terms as being applicable.

(b) ***Late payment on Zero Coupon Notes:***

If the Redemption Amount payable in respect of any Zero Coupon Note is improperly withheld or refused, the Redemption Amount shall thereafter be an amount equal to the sum of:

- (i) the Reference Price; and
- (ii) the product of the Accrual Yield (compounded annually) being applied to the Reference Price on the basis of the relevant Day Count Fraction from (and including) the Issue Date to (but excluding) whichever is the earlier of (i) the day on which all sums due in respect of such Note up to that day are received by or on behalf of the relevant Noteholder and (ii) the day which is seven days after the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent, or, as the case may be, the Trustee has notified the Noteholders that it has received all sums due in respect of the Notes up to such seventh day (except to the extent that there is any subsequent default in payment).

9. **Redemption and Purchase**

(a) ***Scheduled redemption:***

Unless previously redeemed, or purchased and cancelled in accordance with Condition 9(j) (*Cancellation*), the Notes will be redeemed at their Final Redemption Amount on the Maturity Date, subject as provided in Condition 10 (*Payments*).

(b) ***Redemption for tax reasons:***

The Notes may be redeemed at the option of the Issuer in whole, but not in part:

- (i) at any time (if the Floating Rate Note provisions are not specified in the relevant Final Terms as being applicable); or
- (ii) on any Interest Payment Date (if the Floating Rate Note provisions are specified in the relevant Final Terms as being applicable),

on giving not less than 15 nor more than 30 days' notice to the Noteholders (which notice shall be irrevocable), at their Early Redemption Amount (Tax), together with interest accrued (if any) to the date fixed for redemption, if:

- (A) the Issuer has or will become obliged to pay additional amounts as provided or referred to in Condition 11 (*Taxation*) as a result of any change in, or amendment to, the tax laws or regulations of the United Kingdom or any political subdivision or any authority thereof or therein having power to tax, or any change in the application or official interpretation of such laws or regulations (including a holding by a court of competent jurisdiction), which change or amendment becomes effective on or after the date of issue of the first Tranche of the Notes; and

- (B) such obligation cannot be avoided by the Issuer taking reasonable measures available to it,

provided, however, that no such notice of redemption shall be given earlier than:

- (1) where the Notes may be redeemed at any time, 90 days prior to the earliest date on which the Issuer would be obliged to pay such additional amounts if a payment in respect of the Notes were then due; or
- (2) where the Notes may be redeemed only on an Interest Payment Date, 60 days prior to the Interest Payment Date occurring immediately before the earliest date on which the Issuer would be obliged to pay such additional amounts if a payment in respect of the Notes were then due.

Prior to the publication of any notice of redemption pursuant to this paragraph, the Issuer shall deliver to the Trustee (A) a certificate signed by an authorised officer of the Issuer stating that the Issuer is entitled to effect such redemption and setting forth a statement of facts showing that the conditions precedent to the right of the Issuer so to redeem have occurred and (B) an opinion of independent legal advisers of recognised standing to the effect that the Issuer has or will become obliged to pay such additional amounts as a result of such change or amendment. Upon the expiry of any such notice as is referred to in this Condition 9(b), the Issuer shall be bound to redeem the Notes in accordance with this Condition 9(b).

(c) ***Redemption at the option of the Issuer:***

- (i) If Call Option is specified in the relevant Final Terms as being applicable, the Notes may be redeemed at the option of the Issuer in whole or, if so specified in the relevant Final Terms, in part on any Optional Redemption Date (Call) at the relevant Optional Redemption Amount (Call) on the Issuer's giving not less than 15 nor more than 30 days' notice to the Noteholders and the Trustee (which notice shall be irrevocable and shall oblige the Issuer to redeem the Notes or, as the case may be, the Notes specified in such notice on the relevant Optional Redemption Date (Call) at the Optional Redemption Amount (Call) plus accrued interest (if any) to such date).
- (ii) If the Optional Redemption Amount specified in the relevant Final Terms is the "**Make-Whole Redemption Amount**", the amount payable on the relevant Optional Redemption Date will be the higher of:
 - (A) the principal amount of the Notes; and
 - (B) the price, expressed as a percentage of the principal amount of the Notes (rounded to four decimal places with 0.00005 being rounded upwards), at which the then current yield on the Notes on the Reference Date would be equal to the current yield (determined by reference to the middle market price) at the Reference Time on the Reference Date of the relevant Benchmark Security plus the Make-Whole Margin, as determined by the Determination Agent,

provided however that, if the Optional Redemption Date occurs on or after the Par Redemption Date the amount payable on such Optional Redemption Date will be the principal amount of the Notes.

The "**Benchmark Security**", the "**Reference Time**" and the "**Make-Whole Margin**" will be specified in the relevant Final Terms, **provided however that**, if "Linear Interpolation" is specified as applicable in the relevant Final Terms, the current yield of the Benchmark Security shall be determined by linear interpolation (calculated to the nearest one twelfth of a year) of the yield of the two Benchmark Securities specified in the Final Terms.

The "**Reference Date**" means the date which is the third London Business Day prior to the date fixed for redemption.

The "**Determination Agent**" means the agent specified as such in the relevant Final Terms.

(d) ***Partial redemption:***

If the Notes are to be redeemed in part only on any date in accordance with Condition 9(c) (*Redemption at the option of the Issuer*), the Notes to be redeemed shall be selected by the drawing of lots in such place as the Trustee approves and in such manner as the Trustee considers appropriate, subject to compliance with applicable law, the rules of each competent authority, stock exchange and/or quotation system (if any) by which the Notes have then been admitted to listing, trading and/or quotation and the notice to Noteholders referred to in Condition 9(c) (*Redemption at the option of the Issuer*) shall specify the serial numbers of the Notes so to be redeemed. If any Maximum Redemption Amount or Minimum Redemption Amount is specified in the relevant Final Terms, then the Optional Redemption Amount (Call) shall in no event be greater than the maximum or be less than the minimum so specified.

(e) ***Clean-up Call Option***

If Clean-Up Call is specified in the applicable Final Terms and 80 per cent. or more in nominal amount of the Notes originally issued (which shall for this purpose include any further Notes issued and which are consolidated and forming a single Series with one or more previous Tranche(s) of Notes) have been redeemed or purchased and cancelled, the Issuer may, having given: (i) not less than 15 nor more than 30 days' notice to the Noteholders in accordance with Condition 18 (*Notices*); and (ii) not less than 15 days (or such shorter notice as such party shall accept) before the giving of the notice referred to in (i), notice to the Trustee, (which notice shall be irrevocable and shall specify the date fixed for redemption) redeem or, at the Issuer's option, purchase (or procure the purchase of) on any Interest Payment Date (if the relevant Note is a Floating Rate Note) or at any time (if the relevant Note is not a Floating Rate Note), all but not some only of the Notes then outstanding at the Clean-Up Redemption Amount specified in the applicable Final Terms together with interest accrued (if any) to (but excluding) the date fixed for redemption.

(f) ***Redemption at the option of Noteholders:***

If Put Option is specified in the relevant Final Terms as being applicable, the Issuer shall, at the option of the holder of any Note redeem such Note on the Optional Redemption Date (Put) specified in the relevant Put Option Notice at the relevant Optional Redemption Amount (Put) together with interest (if any) accrued to such date. In order to exercise the option contained in this Condition 9(f), the holder of a Note must, not less than 30 nor more than 60 days before the relevant Optional Redemption Date (Put), deposit with any Paying Agent such Note together with all unmatured Coupons relating thereto and a duly completed Put Option Notice in the form obtainable from any Paying Agent. The Paying Agent with which such Note is so deposited shall deliver a duly completed Put Option Receipt to the depositing Noteholder. No Note, once deposited with a duly completed Put Option Notice in accordance with this Condition 9(f), may be withdrawn; **provided, however, that** if, prior to the relevant Optional Redemption Date (Put), any such Note becomes immediately due and payable or, upon due presentation of any such Note on the relevant Optional Redemption Date (Put), payment of the redemption moneys is improperly withheld or refused, the relevant Paying Agent shall mail notification thereof to the depositing Noteholder at such address as may have been given by such Noteholder in the relevant Put Option Notice and shall hold such Note at its Specified Office for collection by the depositing Noteholder against surrender of the relevant Put Option Receipt. For so long as any outstanding Note is held by a Paying Agent in accordance with this Condition 9(f), the depositor of such Note and not such Paying Agent shall be deemed to be the holder of such Note for all purposes.

(g) ***No other redemption:***

The Issuer shall not be entitled to redeem the Notes otherwise than as provided in Conditions 9(a) (*Scheduled redemption*) to 9(f) (*Redemption at the option of Noteholders*) above.

(h) ***Early redemption of Zero Coupon Notes:***

Unless otherwise specified in the relevant Final Terms, the Redemption Amount payable on redemption of a Zero Coupon Note at any time before the Maturity Date shall be an amount equal to the sum of:

- (i) the Reference Price; and
- (ii) the product of the Accrual Yield (compounded annually) being applied to the Reference Price from (and including) the Issue Date to (but excluding) the date fixed for redemption or (as the case may be) the date upon which the Note becomes due and payable.

Where such calculation is to be made for a period which is not a whole number of years, the calculation in respect of the period of less than a full year shall be made on the basis of such Day Count Fraction as may be specified in the Final Terms for the purposes of this Condition 9(h) or, if none is so specified, a Day Count Fraction of 30E/360.

(i) ***Purchase:***

The Issuer or any of its Subsidiaries may at any time purchase Notes in the open market or otherwise and at any price, **provided that** all unmatured Coupons are purchased therewith.

(j) ***Cancellation:***

All Notes so redeemed by the Issuer or any of its Subsidiaries and any unmatured Coupons attached to or surrendered with them shall be cancelled and may not be reissued or resold. Any Notes purchased by the Issuer or any of its Subsidiaries may be cancelled, reissued or resold.

10. **Payments**

(a) ***Principal:***

Payments of principal shall be made only against presentation and (**provided that** payment is made in full) surrender of Notes at the Specified Office of any Paying Agent outside the United States by cheque drawn in the currency in which the payment is due on, or by transfer to an account denominated in that currency (or, if that currency is euro, any other account to which euro may be credited or transferred) and maintained by the payee with, a bank in the Principal Financial Centre of that currency (in the case of a sterling cheque, a town clearing branch of a bank in the City of London).

(b) ***Interest:***

Payments of interest shall, subject to paragraph (h) below, be made only against presentation and (**provided that** payment is made in full) surrender of the appropriate Coupons at the Specified Office of any Paying Agent outside the United States in the manner described in paragraph (a) above.

(c) ***Payments in New York City:***

Payments of principal or interest may be made at the Specified Office of a Paying Agent in New York City if (i) the Issuer has appointed Paying Agents outside the United States with the reasonable expectation that such Paying Agents will be able to make payment of the full amount of the interest on the Notes in the currency in which the payment is due when due, (ii) payment of the full amount of such interest at the offices of all such Paying Agents is illegal

or effectively precluded by exchange controls or other similar restrictions and (iii) payment is permitted by applicable United States law.

(d) ***Payments subject to fiscal laws:***

All payments in respect of the Notes are subject in all cases to any applicable fiscal or other laws and regulations in the place of payment, but without prejudice to the provisions of Condition 11 (*Taxation*). No commissions or expenses shall be charged to the Noteholders or Couponholders in respect of such payments.

(e) ***Deductions for unmatured Coupons:***

If the relevant Final Terms specifies that the Fixed Rate Note provisions are applicable and a Note is presented without all unmatured Coupons relating thereto:

- (i) if the aggregate amount of the missing Coupons is less than or equal to the amount of principal due for payment, a sum equal to the aggregate amount of the missing Coupons will be deducted from the amount of principal due for payment; **provided, however, that** if the gross amount available for payment is less than the amount of principal due for payment, the sum deducted will be that proportion of the aggregate amount of such missing Coupons which the gross amount actually available for payment bears to the amount of principal due for payment;
- (ii) if the aggregate amount of the missing Coupons is greater than the amount of principal due for payment:
 - (A) so many of such missing Coupons shall become void (in inverse order of maturity) as will result in the aggregate amount of the remainder of such missing Coupons (the "**Relevant Coupons**") being equal to the amount of principal due for payment; **provided, however, that** where this subparagraph would otherwise require a fraction of a missing Coupon to become void, such missing Coupon shall become void in its entirety; and
 - (B) a sum equal to the aggregate amount of the Relevant Coupons (or, if less, the amount of principal due for payment) will be deducted from the amount of principal due for payment; **provided, however, that**, if the gross amount available for payment is less than the amount of principal due for payment, the sum deducted will be that proportion of the aggregate amount of the Relevant Coupons (or, as the case may be, the amount of principal due for payment) which the gross amount actually available for payment bears to the amount of principal due for payment.

Each sum of principal so deducted shall be paid in the manner provided in paragraph (a) above against presentation and (**provided that** payment is made in full) surrender of the relevant missing Coupons.

(f) ***Unmatured Coupons void***

If the relevant Final Terms specifies that this Condition 10(f) is applicable or that the Floating Rate Note provisions are applicable, on the due date for final redemption of any Note or early redemption in whole of such Note pursuant to Condition 9(b) (*Redemption for tax reasons*), Condition 9(f) (*Redemption at the option of Noteholders*), Condition 9(c) (*Redemption at the option of the Issuer*), Condition 9(e) (*Clean up Call*) or Condition 12 (*Events of Default*), all unmatured Coupons relating thereto (whether or not still attached) shall become void and no payment will be made in respect thereof.

(g) ***Payments on business days:***

If the due date for payment of any amount in respect of any Note or Coupon is not a Payment Business Day in the place of presentation, the holder shall not be entitled to payment in such place of the amount due until the next succeeding Payment Business Day in such place and shall not be entitled to any further interest or other payment in respect of any such delay.

(h) ***Payments other than in respect of matured Coupons:***

Payments of interest other than in respect of matured Coupons shall be made only against presentation of the relevant Notes at the Specified Office of any Paying Agent outside the United States (or in New York City if permitted by paragraph (c) above).

(i) ***Partial payments:***

If a Paying Agent makes a partial payment in respect of any Note or Coupon presented to it for payment, such Paying Agent will endorse thereon a statement indicating the amount and date of such payment.

(j) ***Exchange of Talons:***

On or after the maturity date of the final Coupon which is (or was at the time of issue) part of a Coupon Sheet relating to the Notes, the Talon forming part of such Coupon Sheet may be exchanged at the Specified Office of the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent for a further Coupon Sheet (including, if appropriate, a further Talon but excluding any Coupons in respect of which claims have already become void pursuant to Condition 13 (*Prescription*)). Upon the due date for redemption of any Note, any unexchanged Talon relating to such Note shall become void and no Coupon will be delivered in respect of such Talon.

(k) ***CMU Service:***

Notwithstanding the foregoing, all payments of principal and interest in respect of Notes held in the CMU Service will be made to the person(s) for whose account(s) interests in the relevant Note are credited as being held with the CMU Service in accordance with the CMU Rules (as defined in the Agency Agreement) at the relevant time as notified to the CMU Lodging Agent by the CMU Service in a relevant CMU Instrument Position Report (as defined in the Agency Agreement) or any other relevant notification by the CMU Service, which notification shall be conclusive evidence of the records of the CMU Service (save in the case of manifest or proven error) and payment made in accordance thereof shall discharge the obligations of the Issuer in respect of that payment.

(l) ***Payment of US Dollar Equivalent:***

The following provisions apply to Notes denominated in Renminbi only. Notwithstanding the foregoing, if by reason of Inconvertibility, Non-transferability or Illiquidity, the Issuer is not able to satisfy payments of principal or interest in respect of Notes denominated in Renminbi when due in Renminbi in Hong Kong, the Issuer may, on giving not less than 10 Hong Kong Banking Days' or more than 30 calendar days' irrevocable notice to the Noteholders prior to the due date for payment, settle any such payment in US Dollars on the due date at the US Dollar Equivalent of any such Renminbi denominated amount.

For the purposes of these Conditions:

"**CMU Service**" means the Central Moneymarkets Unit Service, operated by the Hong Kong Monetary Authority;

"**Renminbi Calculation Agent**" means Deutsche Bank AG, Hong Kong Branch;

"**Renminbi Dealer**" means an independent foreign exchange dealer of international repute active in the Renminbi exchange market in Hong Kong;

"**Determination Business Day**" means a day (other than a Saturday or Sunday) on which commercial banks are open for general business (including dealings in foreign exchange) in Hong Kong, Beijing and in New York City;

"**Determination Date**" means the day which is two Determination Business Days before the due date for any payment of the relevant amount under these Conditions;

"Governmental Authority" means any de facto or de jure government (or any agency or instrumentality thereof), court, tribunal, administrative or other governmental authority or any other entity (private or public) charged with the regulation of the financial markets (including the central bank) of Hong Kong;

"Hong Kong" means the Hong Kong Special Administrative Region of the PRC;

"Hong Kong Banking Day" means a day (other than a Saturday or Sunday) on which commercial banks and foreign exchange markets are generally open for business in Hong Kong for business and settlement of Renminbi.

"Illiquidity" means where the general Renminbi exchange market in Hong Kong becomes illiquid and, as a result of which, the Issuer cannot obtain sufficient Renminbi in order to satisfy its obligation to pay interest and principal (in whole or in part) in respect of the Notes as determined by the Issuer in good faith and in a commercially reasonable manner following consultation (if practicable) with two Renminbi Dealers;

"Inconvertibility" means the occurrence of any event that makes it impossible for the Issuer to convert any amount due in respect of the Notes in the general Renminbi exchange market in Hong Kong, other than where such impossibility is due solely to the failure of the Issuer to comply with any law, rule or regulation enacted by any Governmental Authority (unless such law, rule or regulation is enacted after date of the relevant Final Terms and it is impossible for the Issuer, due to an event beyond its control, to comply with such law, rule or regulation);

"Non-transferability" means the occurrence of any event that makes it impossible for the Issuer to transfer Renminbi between accounts inside Hong Kong or from an account inside Hong Kong to an account outside Hong Kong and outside the PRC or from an account outside Hong Kong and outside the PRC to an account inside Hong Kong, other than where such impossibility is due solely to the failure of the Issuer to comply with any law, rule or regulation enacted by any Governmental Authority (unless such law, rule or regulation is enacted after date of the relevant Final Terms and it is impossible for the Issuer, due to an event beyond its control, to comply with such law, rule or regulation);

"PRC" means the People's Republic of China which, for the purpose of these Conditions, shall exclude Hong Kong, the Macau Special Administrative Region of the People's Republic of China and Taiwan;

"Spot Rate" means the spot CNY/US dollar exchange rate for the purchase of US dollars with Renminbi in the over-the-counter Renminbi exchange market in Hong Kong for settlement in two Determination Business Days, as determined by the Renminbi Calculation Agent at or around 11 a.m. (Hong Kong time) on the Determination Date, on a deliverable basis by reference to Reuters Screen Page TRADCNY3, or if no such rate is available, on a non-deliverable basis by reference to Reuters Screen Page TRADNDF. If neither rate is available, the Renminbi Calculation Agent will determine the Spot Rate at or around 11 a.m. (Hong Kong time) on the Determination Date as the most recently available CNY/U.S. dollar official fixing rate for settlement in two Determination Business Days reported by The State Administration of Foreign Exchange of the PRC, which is reported on the Reuters Screen Page CNY=SAEC. Reference to a page on the Reuters Screen means the display page so designated on the Reuter Monitor Money Rates Service (or any successor service) or such other page as may replace that page for the purpose of displaying a comparable currency exchange rate;

"US Dollar Equivalent" means the Renminbi amount converted into US Dollars using the Spot Rate for the relevant Determination Date; and

"US Dollars" means the lawful currency of the United States of America.

All notifications, opinions, determinations, certificates, calculations, quotations and decisions given, expressed, made or obtained for the purposes of the provisions of this Condition 10(l) by the Renminbi Calculation Agent, will (in the absence of its gross negligence or wilful misconduct) be binding on the Issuer, the Agents and all Noteholders.

11. **Taxation**

(a) ***Gross up:***

All payments of principal and interest in respect of the Notes and the Coupons by or on behalf of the Issuer shall be made free and clear of, and without withholding or deduction for or on account of, any present or future taxes, duties, assessments or governmental charges of whatever nature imposed, levied, collected, withheld or assessed by or on behalf of the United Kingdom or any political subdivision therein or any authority therein or thereof having power to tax, unless the withholding or deduction of such taxes, duties, assessments, or governmental charges is required by law. In that event, the Issuer shall pay such additional amounts as will result in receipt by the Noteholders and the Couponholders after such withholding or deduction of such amounts as would have been received by them had no such withholding or deduction been required, except that no such additional amounts shall be payable in respect of any Note or Coupon presented for payment:

- (i) by or on behalf of a holder which is liable to such taxes, duties, assessments or governmental charges in respect of such Note or Coupon by reason of its having some connection with the jurisdiction by which such taxes, duties, assessments or charges have been imposed, levied, collected, withheld or assessed other than the mere holding of the Note or Coupon; or
- (ii) more than 30 days after the Relevant Date except to the extent that the holder of such Note or Coupon would have been entitled to such additional amounts on presenting such Note or Coupon for payment on the last day of such period of 30 days; or
- (iii) where such withholding or deduction is imposed pursuant to the foreign account tax compliance provisions of the Hiring Incentives to Restore Employment Act of 2010 (commonly referred to as "FATCA"), including the intergovernmental agreement between the United States and the United Kingdom and any laws and regulations enacted pursuant to such agreement.

(b) ***Taxing jurisdiction:***

If the Issuer becomes subject at any time to any taxing jurisdiction other than the United Kingdom, references in these Conditions to the United Kingdom shall be construed as references to the United Kingdom and/or such other jurisdiction.

12. **Events of Default**

If any of the following events occurs and is continuing:

(a) ***Non-payment:***

the Issuer fails to pay any amount of principal in respect of the Notes within seven days of the due date for payment thereof or any amount of interest in respect of the Notes within fourteen days of the due date for payment thereof; or

(b) ***Breach of other obligations:***

the Issuer does not comply in all material respects with any of its other obligations under or in respect of the Notes or the Trust Deed and (except in any case where, in the opinion of the Trustee, such failure is incapable of remedy in which case no continuation or notice as is hereinafter provided will be required) such failure to comply continues unremedied for 30 days (or such longer period as the Trustee may permit) after written notice thereof has been delivered by the Trustee to the Issuer; or

(c) ***Security enforced:***

a secured party takes possession, or a receiver, manager or other similar officer is appointed, of all or substantially all of the undertaking, assets and revenues of the Issuer or any of its Restricted Subsidiaries; or

(d) ***Insolvency etc.:***

(i) the Issuer or any of its Restricted Subsidiaries becomes insolvent or is unable to pay its debts as they fall due, (ii) an administrator or liquidator of the Issuer or any of its Restricted Subsidiaries or all or substantially all of the undertaking, assets and revenues of the Issuer or any of its Restricted Subsidiaries is appointed, (iii) the Issuer or any of its Restricted Subsidiaries or makes a general assignment or an arrangement or composition with or for the benefit of its creditors generally or declares a moratorium in respect of any of its Indebtedness given by it or (iv) the Issuer or any of its Restricted Subsidiaries ceases or threatens to cease to carry on all or any substantial part of its business (otherwise than, in the case of a Subsidiary of the Issuer, for the purposes of or pursuant to an amalgamation, reorganisation or restructuring whilst solvent); or

(e) ***Winding up etc.:***

an order is made or an effective resolution is passed for the winding up, liquidation or dissolution of the Issuer (otherwise than for the purposes of or pursuant to an amalgamation, reorganisation or restructuring whilst solvent on terms previously approved in writing by the Trustee or by an Extraordinary Resolution); or

(f) ***Failure to take action etc.:***

any action, condition or thing at any time required to be taken, fulfilled or done in order (i) to enable the Issuer lawfully to enter into, exercise their respective rights and perform and comply with their respective obligations under and in respect of the Notes, the Coupons and the Trust Deed, (ii) to ensure that those obligations are legal, valid, binding and enforceable and (iii) to make the Notes, the Coupons and the Trust Deed admissible in evidence in the courts of England is not taken, fulfilled or done; or

(g) ***Unlawfulness:***

it is or will become unlawful for the Issuer to perform or comply with any of its obligations under or in respect of the Notes; or

then the Trustee may at its discretion and shall, if so requested in writing by the holders of at least one quarter of the aggregate principal amount of the outstanding Notes, or if so directed by an Extraordinary Resolution (subject to the Trustee having been indemnified or provided with security to its satisfaction) by written notice addressed and delivered to the Issuer, declare the Notes to be immediately due and payable, whereupon they shall become immediately due and payable at their Early Termination Amount together with accrued interest (if any) without further action or formality. Notice of any such declaration shall promptly be given to the Noteholders.

13. **Prescription**

Claims for principal shall become void unless the relevant Notes are presented for payment within ten years of the appropriate Relevant Date. Claims for interest shall become void unless the relevant Coupons are presented for payment within five years of the appropriate Relevant Date.

14. **Replacement of Notes and Coupons**

If any Note or Coupon is lost, stolen, mutilated, defaced or destroyed, it may be replaced at the Specified Office of the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent (and, if the Notes are then admitted to listing, trading and/or quotation by any competent authority, stock exchange and/or quotation system which requires the appointment of a Paying Agent in any particular place, a Paying Agent having its Specified Office in the place required by such competent authority, stock exchange and/or quotation system), subject to all applicable laws and competent authority, stock exchange and/or quotation system requirements, upon payment by the claimant of the expenses incurred in connection with such replacement and on such terms as to evidence, security, indemnity and otherwise as the Issuer may reasonably require. Mutilated or defaced Notes or Coupons must be surrendered before replacements will be issued.

15. **Trustee and Agents**

The Trust Deed contains provisions for the indemnification of the Trustee and for its relief from responsibility, including provisions relieving it from any obligation to take proceedings to enforce repayment unless indemnified and/or secured to its satisfaction and to be paid its costs and expenses in priority to the claims of Noteholders. The Trust Deed also contains provisions pursuant to which the Trustee is entitled, *inter alia*, (i) to enter into business transactions with the Issuer and/or any of its Subsidiaries and/or any related entity thereof and to act as trustee for the holders of any other securities issued or guaranteed by or relating to the Issuer or any of its Subsidiaries, (ii) to exercise and enforce its rights, comply with its obligations and perform its duties under or in relation to any such transactions or, as the case may be, any such trusteeship without regard to the interests of, or consequences for, the Noteholders or Couponholders, and (iii) to retain and not be liable to account for any profit made or any other amount or benefit received thereby or in connection therewith.

In the exercise of its powers and discretions under these Conditions and/or the Trust Deed, the Trustee will have regard to the interests of the Noteholders as a class and will not be responsible for any consequences for individual holders of Notes, Coupons or Talons as a result of such holders being connected in any way with a particular territory or taxing jurisdiction.

In acting under the Agency Agreement and in connection with the Notes and the Coupons, the Paying Agents and the Calculation Agent (if any) act solely as agents of the Issuer or, following the occurrence of an Event of Default, the Trustee and do not assume any obligations towards or relationship of agency or trust for or with any of the Noteholders or Couponholders.

The Principal Paying Agent and the CMU Lodging and Paying Agent and their initial Specified Office is set out below. The initial Calculation Agent (if any) is specified in the relevant Final Terms. The Issuer reserves the right at any time, with the prior written consent of the Trustee, to vary or terminate the appointment of any Paying Agent or Calculation Agent and to appoint a successor principal paying agent, CMU lodging and paying agent or calculation agent and additional or successor paying agents; **provided, however, that:**

- (a) the Issuer shall at all times maintain a Principal Paying Agent and a CMU Lodging and Paying Agent; and
- (b) if a Calculation Agent is specified in the relevant Final Terms, the Issuer shall at all times maintain a Calculation Agent; and
- (c) if and for so long as the Notes are admitted to listing, trading and/or quotation by any competent authority, stock exchange and/or quotation system which requires the appointment of a Paying Agent in any particular place, the Issuer shall maintain a Paying Agent having its Specified Office in the place required by such competent authority, stock exchange and/or quotation system.

Notice of any appointment of, or change in, any of the Paying Agents or in their Specified Offices shall promptly be given to the Noteholders.

16. **Meetings of Noteholders; Modification and Waiver**

- (a) ***Meetings of Noteholders:***

The Trust Deed contains provisions for convening meetings of Noteholders to consider matters relating to the Notes, including the modification of any provision of these Conditions or the Trust Deed. Any such modification may be made if sanctioned by an Extraordinary Resolution. Such a meeting may be convened by the Issuer or the Trustee and shall be convened by the Trustee upon the request in writing of Noteholders holding not less than one-tenth of the aggregate principal amount of the outstanding Notes. The quorum at any meeting convened to vote on an Extraordinary Resolution will be two or more Persons holding or representing one more than half of the aggregate principal amount of the outstanding Notes or, at any adjourned meeting, two or more Persons being or representing Noteholders whatever the principal amount of the Notes held or represented; **provided, however, that** Reserved Matters may only be sanctioned by an Extraordinary Resolution passed at a meeting of Noteholders at which two or more Persons holding or representing not less than three-

quarters or, at any adjourned meeting, not less than one quarter of the aggregate principal amount of the outstanding Notes form a quorum. Any Extraordinary Resolution duly passed at any such meeting shall be binding on all the Noteholders and Couponholders, whether present or not.

In addition, a resolution in writing signed by or on behalf of at least 90 per cent. of the Noteholders who for the time being are entitled to receive notice of a meeting of Noteholders under the Trust Deed will take effect as if it were an Extraordinary Resolution. Such a resolution in writing may be contained in one document or several documents in the same form, each signed by or on behalf of one or more Noteholders.

(b) ***Modification and waiver:***

The Trustee may agree, without the consent of the Noteholders or Couponholders, to (i) any modification to or of these Conditions or the Trust Deed (other than in respect of a Reserved Matter) which is, in the opinion of the Trustee, proper to make if, in the opinion of the Trustee, such modification will not be materially prejudicial to the interests of Noteholders, (ii) any modification of these Conditions and the Notes or the Trust Deed that is of a formal, minor or technical nature or is made to correct a manifest error, and (iii) any waiver or authorisation of any breach or proposed breach, of any of the provisions of these Conditions or the Trust Deed (other than a proposed breach or breach relating to the subject of a Reserved Matter) that is in the opinion of the Trustee not materially prejudicial to the interests of the Noteholders. Any such modification, authorisation or waiver shall be binding on the Noteholders and the Couponholders and, if the Trustee so requires, such modification, authorisation or waiver shall be notified to the Noteholders as soon as practicable in accordance with Condition 18 (*Notices*).

Additionally, the Issuer may in accordance with Condition 7(i) (*Benchmark Discontinuation*), vary or amend these Conditions, the Trust Deed and/or the Agency Agreement to give effect to certain amendments without any requirement for the consent or approval of Noteholders or Couponholders, as described in Condition 7(i) (*Benchmark Discontinuation*) and the Trustee shall agree to such variations or amendments subject to the terms of Condition 7(i) (*Benchmark Discontinuation*), or as otherwise notified to Noteholders and Couponholders.

(c) ***Substitution:***

The Trust Deed contains provisions under which any Subsidiary of the Issuer may, without the consent of the Noteholders or Couponholders assume the obligations of the Issuer as principal debtor under the Trust Deed and the Notes **provided that** certain conditions specified in the Trust Deed are fulfilled.

No Noteholder or Couponholder shall, in connection with any substitution, be entitled to claim any indemnification or payment in respect of any tax consequence thereof for such Noteholder or (as the case may be) Couponholder except to the extent provided for in Condition 11 (*Taxation*) (or any undertaking given in addition to or substitution for it pursuant to the provisions of the Trust Deed).

17. **Enforcement**

The Trustee may, at any time, at its discretion and without further notice, institute such proceedings against the Issuer as it thinks fit to enforce any obligation, condition or provision binding on the Issuer under these Conditions or under the Trust Deed in respect of the Notes, but shall not be bound to do so unless:

- (a) it has been so directed by an Extraordinary Resolution or it has been so requested in writing by the holders of at least one quarter of the nominal amount of the Notes outstanding; and
- (b) it has been indemnified and/or secured to its satisfaction.

No Noteholder or Couponholder shall be entitled to institute proceedings directly against the Issuer unless the Trustee, having become bound to proceed as aforesaid, fails to do so within a reasonable time and such failure is continuing.

18. **Notices**

(a) ***Valid Notices:***

Notices to the Noteholders shall be valid if published in a leading English language daily newspaper published in London (which is expected to be the *Financial Times*) or, in the case of Renminbi Notes cleared through the CMU, published in Asia or, if such publication is not practicable, in a leading English language daily newspaper having general circulation in Europe or Asia (as the case may be). Any such notice shall be deemed to have been given on the date of first publication (or if required to be published in more than one newspaper, on the first date on which publication shall have been made in all the required newspapers).

(b) ***Other Methods:***

Notwithstanding paragraph (a) above, the Trustee may approve some other method of giving notice to the Noteholders if, in its opinion, that other method is reasonable having regard to market practice then prevailing and to the requirements of any stock exchange on which Notes are then listed and **provided that** notice of that other method is given to the Noteholders in the manner required by the Trustee.

(c) ***Couponholders:***

Couponholders shall be deemed for all purposes to have notice of the contents of any notice given to the Noteholders.

19. **Rounding**

For the purposes of any calculations referred to in these Conditions (unless otherwise specified in these Conditions or the relevant Final Terms), (a) all percentages resulting from such calculations will be rounded, if necessary, to the nearest one hundred-thousandth of a percentage point (with 0.000005 per cent. being rounded up to 0.00001 per cent.), (b) all United States dollar amounts used in or resulting from such calculations will be rounded to the nearest cent (with one half cent being rounded up), (c) all Japanese Yen amounts used in or resulting from such calculations will be rounded downwards to the next lower whole Japanese Yen amount, and (d) all amounts denominated in any other currency used in or resulting from such calculations will be rounded to the nearest two decimal places in such currency, with 0.005 being rounded upwards.

20. **Governing Law and Jurisdiction**

(a) ***Governing Law:***

The Notes and the Trust Deed and any non-contractual obligations arising out of or in connection with the Notes and the Trust Deed are governed by English law.

(b) ***Jurisdiction:***

The parties to the Trust Deed have (i) agreed that the courts of England have exclusive jurisdiction to settle any dispute (a "**Dispute**"), arising out of or in connection with the Trust Deed or the Notes (including a dispute regarding the existence, validity or termination of the Trust Deed or the Notes and all non-contractual obligations arising out of or in connection with them) or the consequences of their nullity; and (ii) agreed that those courts are the most appropriate and convenient courts to settle any Dispute and, accordingly, that they will not argue to the contrary. Notwithstanding the above, the Trustee or any of the Noteholders may take proceedings relating to a Dispute ("**Proceedings**") in any other courts with jurisdiction. To the extent allowed by law, the Trustee or any of the Noteholders may take concurrent Proceedings in any number of jurisdictions.

FORM OF FINAL TERMS

[PROHIBITION OF SALES TO EEA RETAIL INVESTORS - The Notes are not intended to be offered, sold or otherwise made available to and should not be offered, sold or otherwise made available to any retail investor in the European Economic Area ("EEA"). For these purposes, a retail investor means a person who is one (or more) of: (i) a retail client as defined in point (11) of Article 4(1) of Directive 2014/65/EU (as amended, "MiFID II"); or (ii) a customer within the meaning of Directive 2002/92/EC, as amended or superseded, where that customer would not qualify as a professional client as defined in point (10) of Article 4(1) of MiFID II. No key information document required by Regulation (EU) No 1286/2014 (the "PRIIPs Regulation") for offering or selling the Notes or otherwise making them available to retail investors in the EEA has been prepared and therefore offering or selling the Notes or otherwise making them available to any retail investor in the EEA may be unlawful under the PRIIPs Regulation.]

[MiFID II product governance/Professional investors and ECPs only target market – Solely for the purposes of [the/each] manufacturer's product approval process, the target market assessment in respect of the Notes has led to the conclusion that: (i) the target market for the Notes is eligible counterparties and professional clients only, each as defined in [Directive 2014/65/EU (as amended, "MiFID II")/MiFID II]; and (ii) all channels for distribution of the Notes to eligible counterparties and professional clients are appropriate. Any person subsequently offering, selling or recommending the Notes (a "distributor") should take into consideration the manufacturer['s/s'] target market assessment; however, a distributor subject to MiFID II is responsible for undertaking its own target market assessment in respect of the Notes (by either adopting or refining the manufacturer['s/s'] target market assessment) and determining appropriate distribution channels.]

[Singapore Securities and Futures Act Product Classification – Solely for the purposes of its obligations pursuant to sections 309B(1)(a) and 309B(1)(c) of the Securities and Futures Act (Chapter 289 of Singapore) (the "SFA"), the Issuer has determined, and hereby notifies all relevant persons (as defined in Section 309A of the SFA) that the Notes are ["prescribed capital markets products "]/["capital markets products other than prescribed capital markets products"] (as defined in the Securities and Futures (Capital Markets Products) Regulations 2018) and ["Excluded Investment Products "]/["Specified Investment Products"] (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).]

Final Terms dated [•]

AstraZeneca PLC
Legal Entity Identifier (LEI): PY6ZZQWO2IZFZC3IOL08
Issue of [Aggregate Nominal Amount of Tranche] [Title of Notes]
under the US\$10,000,000,000
Euro Medium Term Note Programme

PART A — CONTRACTUAL TERMS

[Terms used herein shall be deemed to be defined as such for the purposes of the Conditions (the "Conditions") set forth in the base prospectus dated 12 June 2019 [and the supplemental base prospectus dated [•]] which [together] constitute[s] a base prospectus (the "Base Prospectus") for the purposes of the Prospectus Directive (as defined below). This document constitutes the Final Terms of the Notes described herein for the purposes of Article 5.4 of the Prospectus Directive. These Final Terms contain the final terms of the Notes and must be read in conjunction with the Base Prospectus.

Full information on the Issuer and the offer of the Notes described herein is only available on the basis of the combination of these Final Terms and the Base Prospectus [as so supplemented]. The Base Prospectus [and the supplemental base prospectus] [is] [are] available for viewing [at the website of the London Stock Exchange (www.londonstockexchange.com)] [and] during normal business hours at [•] [and copies may be obtained from [•]].]

[Terms used herein shall be deemed to be defined as such for the purposes of the Conditions (the "Conditions") set forth in the base prospectus dated [5 May 2016 / 21 June 2018] and which are incorporated by reference in the Base Prospectus dated 12 June 2019. This document constitutes the Final Terms of the Notes described herein for the purposes of Article 5.4 of the Prospectus Directive (as defined below) and must be read in conjunction with the Base Prospectus dated 12 June 2019 [and the supplemental base prospectus dated [•]] which [together] constitute[s] a base prospectus (the "Base Prospectus") for the purposes of the Prospectus

Directive, save in respect of the Conditions which are set forth in the base prospectus dated [5 May 2016 / 21 June 2018] and are incorporated by reference in the Base Prospectus.

Full information on the Issuer and the offer of the Notes described herein is only available on the basis of the combination of these Final Terms and the Base Prospectus [as so supplemented]. The Base Prospectus [and the supplemental base prospectus] [is] [are] available for viewing [at the website of the London Stock Exchange (www.londonstockexchange.com)] [and] during normal business hours at [•] [and copies may be obtained from [•]].]

In these Final Terms, the expression "**Prospectus Directive**" means Directive 2003/71/EC (as amended or superseded) and includes any relevant implementing measures in the Relevant Member State.

1. Issuer: AstraZeneca PLC
2. (i) Series Number: [•]
(ii) Tranche Number: [•]
3. Specified Currency or Currencies: [•]
4. Aggregate Nominal Amount:
(i) Series: [•]
(ii) [Tranche: [•]
5. Issue Price: [•] per cent. of the Aggregate Nominal Amount [plus accrued interest from [•]]
6. (i) Specified Denominations: [•] [and integral multiples of EUR [•] in excess thereof up to and including EUR [•]. Definitive Notes will not be issued in denominations in excess of EUR [•].
(ii) Calculation Amount: [•]
7. (i) Issue Date: [•]
(ii) Interest Commencement Date: [•] / [Issue Date] / [Not Applicable]
8. Maturity Date: [•]
9. Interest Basis: [[•] per cent. Fixed Rate]
[[•] month EURIBOR/LIBOR] +/- [•] per cent. Floating Rate]
[Zero Coupon]
10. Redemption/Payment Basis: [Redemption at par]
11. Change of Interest or Redemption/Payment Basis: [[•]/Not Applicable]
12. Put/Call Options: [Investor Put]
[Issuer Call]
[Not Applicable]
13. (i) Status of the Notes: Senior

[(ii)] [Date [Board] approval for issuance of Notes obtained: [•]

PROVISIONS RELATING TO INTEREST (IF ANY) PAYABLE

14. **Fixed Rate Note Provisions** [Applicable/Not Applicable]
- (i) Rate[(s)] of Interest: [•] per cent. per annum payable in arrear on each Interest Payment Date
 - (ii) Interest Payment Date(s): [•] in each year
 - (iii) Fixed Coupon Amount[(s)]: [•] per Calculation Amount
 - (iv) Broken Amount(s): [[•] per Calculation Amount payable on the Interest Payment Date falling [in/on] [•]]
 - (v) Day Count Fraction: [30/360/Actual/Actual(ICMA)/Actual/Actual (ISDA)]
 - [(vi)] Determination Dates: [•] in each year [[•]]
15. **Floating Rate Note Provisions** [Applicable/Not Applicable]
- (i) Interest Period(s): [•]
 - [(ii)] Specified Period: [[•]/[Not Applicable]]
 - (iii) Specified Interest Payment Dates: [•]
 - (iv) First Interest Payment Date: [•]
 - (v) Business Day Convention: [Floating Rate Convention/Following Business Day Convention/Modified Following Business Day Convention/Preceding Business Day Convention/No Adjustment]
 - (vi) Additional Business Centre(s): [Not Applicable/[•]]
 - (vii) Manner in which the Rate(s) of Interest is/are to be determined: [Screen Rate Determination/ISDA Determination]
 - (viii) Party responsible for calculating the Rate(s) of Interest and Interest Amount(s) (if not the [Principal Paying Agent/ CMU Lodging and Paying Agent]): [[•]/[Not Applicable]]
 - (ix) Screen Rate Determination:
 - Reference Rate: [[•] month EURIBOR/LIBOR]
 - Interest Determination Date(s): [•]
 - Relevant Screen Page: [•]
 - Relevant Time: [•]
 - Relevant Financial Centre: [•]
 - (x) ISDA Determination:

	• Floating Rate Option:	[•]
	• Designated Maturity:	[•]
	• Reset Date:	[•]
	• ISDA Benchmarks Supplement:	[Applicable/Not Applicable]
(xi)	Margin(s):	[+/-][•] per cent. per annum
(xii)	Minimum Rate of Interest:	[[•] per cent. per annum]/[Not Applicable]
(xiii)	Maximum Rate of Interest:	[[•] per cent. per annum]/[Not Applicable]
(xiv)	Day Count Fraction:	[Actual / Actual (ICMA) / Actual/Actual (ISDA) / Actual/365 (Fixed) / Actual/360 / 30/360 / 30E/360 / Eurobond Basis / 30E/360 (ISDA)]
(xv)	Determination Agent:	[[•]/Not Applicable]
16.	Zero Coupon Note Provisions	[Applicable/Not Applicable]
(i)	[Amortisation/Accrual] Yield:	[•] per cent. per annum
(ii)	Reference Price:	[•]
(iii)	Any other formula/basis of determining amount payable:	[[•]]

PROVISIONS RELATING TO REDEMPTION

17.	Call Option	[Applicable/Not Applicable]
(i)	Optional Redemption Date(s):	[•]
(ii)	Optional Redemption Amount(s) of each Note and method, if any, of calculation of such amount(s):	[•] per Calculation Amount/Make-Whole Redemption Amount/[•]
(iii)	If redeemable in part:	
	(a) Minimum Redemption Amount:	[•] per Calculation Amount
	(b) Maximum Redemption Amount:	[•] per Calculation Amount
(iv)	Notice period:	[•]
(v)	[Benchmark Security] [Benchmark Securities]:	[•]
(vi)	Reference Time:	[•]
(vii)	Make-Whole Margin:	[•]
(viii)	Linear Interpolation:	[Applicable/Not Applicable]
(ix)	Par Redemption Date:	[[•]/Not Applicable]
(x)	Clean-up Call:	[Applicable/Not Applicable]

- | | | |
|------|---|------------------------------|
| (xi) | Clean-up Redemption Amount | [[•]/Not Applicable] |
| 18. | Put Option | [Applicable/Not Applicable] |
| | (i) Optional Redemption Date(s): | [•] |
| | (ii) Notice period: | [•] |
| 19. | Final Redemption Amount of each Note | [[•] per Calculation Amount] |
| 20. | Early Termination Amount | |
| | Early Redemption Amount (Tax) and Early Termination Amount per Calculation Amount payable on redemption for taxation reasons or, as the case may be, on event of default: | [•][Not Applicable] |

GENERAL PROVISIONS APPLICABLE TO THE NOTES

- | | | |
|-----|---|--|
| 21. | Form of Notes: | [Temporary Global Note exchangeable for a Permanent Global Note which is exchangeable for Definitive Notes on [•] days' notice/at any time/in the limited circumstances specified in the Permanent Global Note.] |
| | | [Temporary Global Note exchangeable for Definitive Notes on [•] days' notice.] |
| | | [Permanent Global Note exchangeable for Definitive Notes on [•] days' notice/at any time/in the limited circumstances specified in the Permanent Global Note]. |
| 22. | New Global Note Form: | [Applicable/Not Applicable] |
| 23. | Additional Financial Centre(s) or other special provisions relating to Payment Dates: | [Not Applicable/[•]] |
| 24. | Talons for future Coupons or Receipts to be attached to Definitive Notes (and dates on which such Talons mature): | [Yes/No.] |
| 25. | [Consolidation provisions: | [Not Applicable] |

Signed on behalf of the Issuer:

By:
Duly authorised

PART B — OTHER INFORMATION

1. LISTING AND ADMISSION TO TRADING

- (i) Admission to trading: Application [has been/is expected to be] made by the Issuer (or on its behalf) for the Notes to be admitted to trading on the Regulated Market of the London Stock Exchange plc with effect from [•].
- (ii) Estimate of total expenses related to admission to trading: [•]

2. RATINGS

- Ratings: The Notes to be issued [have been/are expected to be] rated:
- [S&P Global Ratings Europe Limited, UK Branch: [•]]
- [Moody's France SAS: [•]]
- [Not Applicable]
- [[•] is established in the EEA and registered under Regulation (EU) No 1060/2009, as amended.]
- [[•] is established in the EEA and has applied for registration under Regulation (EU) No 1060/2009, as amended, although notification of the corresponding registration decision has not yet been provided by the [relevant competent authority] / [European Securities and Markets Authority].]
- [[•] is established in the EEA and is neither registered nor has it applied for registration under Regulation (EU) No 1060/2009, as amended.]
- [[•] is not established in the EEA but the rating it has given to the Notes is endorsed by [•], which is established in the EEA and registered under Regulation (EU) No 1060/2009, as amended.]
- [[•] is not established in the EEA but is certified under Regulation (EU) No 1060/2009, as amended.]
- [[•] is not established in the EEA and is not certified under Regulation (EU) No 1060/2009, as amended (the "**CRA Regulation**") and the rating it has given to the Notes is not endorsed by a credit rating agency established in the EEA and registered under the CRA Regulation.]

3. INTERESTS OF NATURAL AND LEGAL PERSONS INVOLVED IN THE ISSUE/OFFER

[Save as discussed in "*Subscription and Sale*" in the Base Prospectus, so far as the Issuer is aware, no person involved in the offer of the Notes has an interest material to the offer.]/[•]/[Not Applicable]

4. [Fixed Rate Notes Only] — YIELD

- Indication of yield: [•]

5. **OPERATIONAL INFORMATION**

ISIN Code:	[•]
Common Code:	[•]
[FISN	[See the website of the Association of National Numbering Agencies (ANNA) or alternatively source from the responsible National Numbering Agency that assigned the ISIN /Not Applicable / Not Available]
[CFI Code	[See the website of the Association of National Numbering Agencies (ANNA) or alternatively source from the responsible National Numbering Agency that assigned the ISIN / Not Applicable / Not Available]
	<i>(If the FISN and/or CFI code is not required or requested, it/they should be specified to be "Not Applicable")</i>
Any clearing system(s) other than Euroclear Bank SA/NV and Clearstream Banking S.A. and the relevant identification number(s):	[Not Applicable / [•]]
New Global Note intended to be held in a manner which would allow Eurosystem eligibility:	[Not Applicable]
	[Yes. Note that the designation "Yes" simply means that the Notes are intended upon issue to be deposited with one of the ICSDs as common safekeeper and does not necessarily mean that the Notes will be recognised as eligible collateral for Eurosystem monetary policy and intra-day credit operations by the Eurosystem either upon issue or at any or all times during their life. Such recognition will depend upon the European Central Bank being satisfied that Eurosystem eligibility criteria have been met.]
	[No. Whilst the designation is specified as "No" at the date of this Final Terms, should the Eurosystem eligibility criteria be amended in the future such that the Notes are capable of meeting them, the Notes may then be deposited with one of the ICSDs as common safekeeper. Note that this does not necessarily means that the Notes will then be recognised as eligible collateral for Eurosystem monetary policy and intra-day credit operations by the Eurosystem at any time during their life. Such recognition will depend upon the European Central Bank being satisfied that Eurosystem eligibility criteria have been met.]
Delivery:	Delivery [against/free of] payment
Names and addresses of additional paying agent(s) (if any):	[•]
Relevant Benchmark[s]:	[[specify benchmark] is provided by [administrator legal name]][repeat as necessary]. As at the date hereof, [[administrator legal name][appears]/[does

not appear][*repeat as necessary*] in the register of administrators and benchmarks established and maintained by ESMA pursuant to Article 36 (*Register of administrators and benchmarks*) of the Benchmark Regulation]/[As far as the Issuer is aware, as at the date hereof, [*specify benchmark*] does not fall within the scope of the Benchmark Regulation]/ [As far as the Issuer is aware, the transitional provisions in Article 51 of Regulation (EU) 2016/1011, as amended apply, such that [*name of administrator*] is not currently required to obtain authorisation/registration (or, if located outside the European Union, recognition, endorsement or equivalence)]/ [Not Applicable]

Prohibition of Sales to EEA Retail Investors:

[Applicable / Not Applicable]

TEFRA:

[Not Applicable/The [C/D] Rules are applicable]

6. **[THIRD PARTY INFORMATION]**

[[•] has been extracted from [•]. The Issuer confirms that such information has been accurately reproduced and that, so far as it is aware, and is able to ascertain from information published by [•], no facts have been omitted which would render the reproduced inaccurate or misleading.

SUMMARY OF PROVISIONS RELATING TO THE NOTES WHILE IN GLOBAL FORM

Clearing System Accountholders

Each Global Note will be in bearer form. Consequently, in relation to any Tranche of Notes represented by a Global Note, references in the Terms and Conditions of the Notes to "Noteholder" are references to the bearer of the relevant Global Note which, for so long as the Global Note is held (i) in the case of a Global Note not lodged with CMU, by a depository or a common depository, in the case of a CGN, or a common safekeeper, in the case of an NGN for Euroclear and/or Clearstream and/or any other relevant clearing system, will be that depository or common depository or, as the case may be, common safekeeper, or (ii) in the case of a Global Note lodged with CMU, a sub-custodian for CMU.

Each of the persons shown in the records of Euroclear, Clearstream and/or CMU and/or any other relevant clearing system as being entitled to an interest in a Global Note (each an "**Accountholder**") must look solely to Euroclear, Clearstream and/or CMU and/or such other relevant clearing system (as the case may be) for such Accountholder's share of each payment made by the Issuer to the bearer of such Global Note and in relation to all other rights arising under the Global Note. The extent to which, and the manner in which, Accountholders may exercise any rights arising under the Global Note will be determined by the respective rules and procedures of the relevant Clearing System(s) and any other relevant clearing system from time to time. For so long as the relevant Notes are represented by the Global Note, Accountholders shall have no claim directly against the Issuer in respect of payments due under the Notes and such obligations of the Issuer will be discharged by payment to the bearer of the Global Note.

Exchange of Temporary Global Notes

Whenever any interest in a Temporary Global Note is to be exchanged for an interest in a Permanent Global Note, the Issuer shall procure:

- (a) in the case of first exchange, the prompt delivery (free of charge to the bearer) of such Permanent Global Note, duly authenticated and, in the case of an NGN, effectuated, to the bearer of the Temporary Global Note; or
- (b) in the case of any subsequent exchange, an increase in the principal amount of such Permanent Global Note in accordance with its terms,

in each case in an aggregate principal amount equal to the aggregate of the principal amounts specified in the certificates issued by the relevant Clearing System(s) and/or any other relevant clearing system and received by the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent against presentation and (in the case of final exchange) surrender of the Temporary Global Note to or to the order of the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent within 7 days of the bearer requesting such exchange.

Whenever a Temporary Global Note is to be exchanged for Definitive Notes, the Issuer shall procure the prompt delivery (free of charge to the bearer) of such Definitive Notes, duly authenticated and with Coupons and Talons attached (if so specified in the relevant Final Terms), in an aggregate principal amount equal to the principal amount of the Temporary Global Note to the bearer of the Temporary Global Note against the surrender of the Temporary Global Note to or to the order of the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent within 30 days of the bearer requesting such exchange.

If:

- (a) a Permanent Global Note has not been delivered or the principal amount thereof increased by 5.00 p.m. (London time or, in the case of Notes lodged with CMU, Hong Kong time) on the seventh day after the bearer of a Temporary Global Note has requested exchange of an interest in the Temporary Global Note for an interest in a Permanent Global Note; or
- (b) Definitive Notes have not been delivered by 5.00 p.m. (London time or, in the case of Notes lodged with CMU, Hong Kong time) on the thirtieth day after the bearer of a Temporary Global Note has requested exchange of the Temporary Global Note for Definitive Notes; or
- (c) a Temporary Global Note (or any part thereof) has become due and payable in accordance with the Terms and Conditions of the Notes or the date for final redemption of a Temporary Global Note has

occurred and, in either case, payment in full of the amount of principal falling due with all accrued interest thereon has not been made to the bearer of the Temporary Global Note in accordance with the terms of the Temporary Global Note on the due date for payment,

then the Temporary Global Note (including the obligation to deliver a Permanent Global Note or increase the principal amount thereof or deliver Definitive Notes, as the case may be) will become void at 5.00 p.m. (London time or, in the case of Notes lodged with CMU, Hong Kong time) on such seventh day (in the case of (a) above) or at 5.00 p.m. (London time or, in the case of Notes lodged with CMU, Hong Kong time) on such thirtieth day (in the case of (b) above) or at 5.00 p.m. (London time or, as the case may be, Hong Kong time) on such due date (in the case of (c) above) and the bearer of the Temporary Global Note will have no further rights thereunder.

Exchange of Permanent Global Notes

Whenever a Permanent Global Note is to be exchanged for Definitive Notes, the Issuer shall procure the prompt delivery (free of charge to the bearer) of such Definitive Notes, duly authenticated and with Coupons and Talons attached (if so specified in the relevant Final Terms), in an aggregate principal amount equal to the principal amount of the Permanent Global Note to the bearer of the Permanent Global Note against the surrender of the Permanent Global Note to or to the order of the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent within 30 days of the bearer requesting such exchange.

If:

- (a) Definitive Notes have not been delivered by 5.00 p.m. (London time or, in the case of Notes lodged with CMU, Hong Kong time) on the thirtieth day after the bearer of a Permanent Global Note has duly requested exchange of the Permanent Global Note for Definitive Notes; or
- (b) a Permanent Global Note (or any part of it) has become due and payable in accordance with the Terms and Conditions of the Notes or the date for final redemption of the Notes has occurred and, in either case, payment in full of the amount of principal falling due with all accrued interest thereon has not been made to the bearer of the Permanent Global Note in accordance with the terms of the Permanent Global Note on the due date for payment,

then the Permanent Global Note (including the obligation to deliver Definitive Notes) will become void at 5.00 p.m. (London time or, in the case of Notes lodged with CMU, Hong Kong time) on such thirtieth day (in the case of (a) above) or at 5.00 p.m. (London time or, in the case of Notes lodged with CMU, Hong Kong time) on such due date (in the case of (b) above) and the bearer of the Permanent Global Note will have no further rights thereunder.

Conditions applicable to Global Notes

Each Global Note will contain provisions which modify the Terms and Conditions of the Notes as they apply to the Global Note. The following is a summary of certain of those provisions:

Payments:

All payments in respect of the Global Note will be made against presentation and (in the case of payment of principal in full with all interest accrued thereon) surrender of the Global Note to or to the order of any Paying Agent and will be effective to satisfy and discharge the corresponding liabilities of the Issuer in respect of the Notes. On each occasion on which a payment of principal or interest is made in respect of the Global Note, the Issuer shall procure that in respect of a CGN the payment is noted in a schedule thereto and in respect of an NGN the payment is entered *pro rata* in the records of Euroclear and Clearstream.

Exercise of put option:

In order to exercise the option contained in Condition 9(f) (*Redemption at the option of Noteholders*) the bearer of the Permanent Global Note must, within the period specified in the Conditions for the deposit of the relevant Note and put notice, give written notice of such exercise to the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent specifying the principal amount of Notes in respect of which such option is being exercised. Any such notice will be irrevocable and may not be withdrawn.

Payment Business Day

In the case of a Global Note, shall be: if the currency of payment is euro, any day which is a TARGET Settlement Day and a day on which dealings in foreign currencies may be carried on in each (if any) Additional Financial Centre; or, if the currency of payment is not euro, any day which is a day on which dealings in foreign currencies may be carried on in the Principal Financial Centre of the currency of payment and in each (if any) Additional Financial Centre.

Partial exercise of call option:

In connection with an exercise of the option contained in Condition 9(c) (*Redemption at the option of the Issuer*) in relation to some only of the Notes, the Permanent Global Note may be redeemed in part in the principal amount specified by the Issuer in accordance with the Conditions and the Notes to be redeemed will not be selected as provided in the Conditions but in accordance with the rules and procedures of the relevant Clearing System(s) (to be reflected in the records of the relevant Clearing System(s) as either a pool factor or a reduction in principal amount, at their discretion).

Notices:

Notwithstanding Condition 18 (*Notices*), while all the Notes are represented by a Permanent Global Note (or by a Permanent Global Note and/or a Temporary Global Note) and the Permanent Global Note is (or the Permanent Global Note and/or the Temporary Global Note are) deposited with a depositary or a common depositary for Euroclear and/or Clearstream and/or lodged with a sub-custodian for CMU and/or any other relevant clearing system or a common safekeeper (as the case may be), notices to Noteholders may be given by delivery of the relevant notice to Euroclear, Clearstream and/or CMU and/or any other relevant clearing system (as the case may be) and, in any case, such notices shall be deemed to have been given to the Noteholders in accordance with Condition 18 (*Notices*) on the date of delivery to Euroclear, Clearstream and/or CMU and/or any other relevant clearing system.

USE OF PROCEEDS

The net proceeds from the issue of each Tranche of Notes will be used for the general corporate purposes of the Issuer's business which may include the repayment of debt.

DESCRIPTION OF THE ISSUER

Introduction

AstraZeneca PLC (the "**Issuer**" or "**AstraZeneca**") was formed on 6 April 1999 from the merger of Astra AB of Sweden and Zeneca Group PLC of the United Kingdom. The Issuer's registered office is situated at 1 Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge CB2 0AA, telephone number: +44 20 3749 5000, facsimile number: +44 1223 352858. The registered number of the Issuer is 2723534.

This business description set out in this section of this Base Prospectus is an overview of, is qualified in its entirety by, and should be read in conjunction with, the information incorporated by reference into this Base Prospectus (see "*Documents incorporated by reference*").

Principal Activities

AstraZeneca is a global, science-led, pharmaceutical business delivering medicines to patients through innovative science and excellence in development and commercialisation in three main therapy areas: oncology, cardiovascular, renal and metabolism ("**CVRM**") and respiratory. AstraZeneca is also selectively active in the areas of autoimmunity, neuroscience and infection.

AstraZeneca has activities in over 100 countries worldwide, with three strategic Research & Development ("**R&D**") centres in Sweden, the UK and the US and operations sites in 17 countries. As at 31 December 2018, it employed approximately 64,600 people (approximately 29.0 per cent. in Europe, 43.7 per cent. in Emerging Markets (as defined in the Annual Report and Form 20-F Information 2018), 19.8 per cent. in the US and 7.5 per cent. in Australia and New Zealand, Canada and Japan (the "**Established Rest of World**").

Key Products

AstraZeneca has a broad range of marketed medicines that continue to make a positive difference in healthcare. In addition to its pipeline of products in the discovery and development phases, AstraZeneca's pipeline includes life-cycle management initiatives for approved products to bring further benefit for patients and maximise their commercial potential.

Oncology medicines

AstraZeneca's key marketed oncology products include:

- *Tagrisso* (osimertinib), an epidermal growth factor receptor ("**EGFR**") tyrosine kinase inhibitor indicated for patients with metastatic EGFR T790M mutation-positive NSCLC;
- *Lynparza* (olaparib), an oral ADP-ribose polymerase inhibitor approved in the European Union (the "**EU**") for the treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (germline and/or somatic) high-grade serious epithelial ovarian, fallopian tube or primary peritoneal cancer and approved in the US for the treatment of patients with germline BRCA-mutated advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy;
- *Imfinzi* (durvalumab), approved by the US Food and Drug Administration ("**FDA**") for the treatment of locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy, or where the disease has progressed within 12 months of receiving platinum-containing chemotherapy before or after surgery and for the treatment of locally advanced, unresectable NSCLC whose disease has not progressed following platinum-based chemoradiation therapy;
- *Calquence* (acalabrutinib), granted accelerated approval by the FDA in October 2017, as a treatment for relapsed or refractory mantle cell lymphoma;
- *Lumoxiti* (moxetumomab pasudotox-tdfk), approved in the US for third line relapsed or refractory Hairy Cell Leukaemia ("**HCL**");
- *Iressa* (gefitinib), an epidermal growth factor receptor-tyrosine kinase inhibitor that acts to block signals for cancer cell growth and survival in non-small cell lung cancer ("**NSCLC**");

- *Faslodex* (fulvestrant), an injectable oestrogen receptor antagonist for the treatment of breast cancer;
- *Zoladex* (goserelin acetate implant), for the treatment of prostate cancer, breast cancer and certain benign gynaecological disorders;
- *Arimidex* (anastrozole), an aromatase inhibitor for the treatment of breast cancer; and
- *Casodex* (bicalutamide), an anti-androgen therapy for the treatment of prostate cancer.

In 2015 and 2016, AstraZeneca continued to build its oncology business by investing in a robust clinical development programme and by making strategic partnerships and acquisitions, such as acquiring a majority equity stake in Acerta Pharma to establish its footprint in haematology.

In 2017, AstraZeneca created the Oncology Business Unit ("**OBU**") focused on eight key markets, with the aim of accelerating the uptake of its new medicines through strategic focus, quick decision making, and adequate investments.

In 2018, based on the commercial uptake of its new medicines, and the maturity of their late-stage clinical programmes, AstraZeneca organised the OBU into five franchises: *Tagrisso*, *Imfinzi*, *Lynparza*, *Calquence* and its mature portfolio (comprised of *Faslodex*, *Zoladex* and *Iressa*).

Cardiovascular, renal and metabolism medicines

AstraZeneca's key marketed CVRM products include:

- *Brilinta/Brilique* (ticagrelor), an oral antiplatelet for the treatment of acute coronary syndromes;
- *Farxiga/Forxiga* (dapagliflozin), a selective inhibitor of human sodium-glucose co-transporter 2 to improve glycaemic control in adult patients with Type 2 diabetes mellitus;
- *Onglyza* (saxagliptin), an oral dipeptidyl peptidase 4 inhibitor for Type 2 diabetes mellitus;
- *Bydureon* (exenatide XR injectable suspension), an injectable medicine indicated to improve blood sugar (glucose), along with diet and exercise in adults with Type 2 diabetes mellitus;
- *Byetta* (exenatide injection), a twice-daily injectable medicine indicated to improve blood sugar (glucose) control, along with diet and exercise in adults with Type 2 diabetes mellitus;
- *Symlin* (pramlintide acetate), an injected amylin analogue for Type 1 and Type 2 diabetes mellitus in patients with inadequate glycaemic control on meal time insulin;
- *Crestor* (rosuvastatin calcium), for the treatment of dyslipidaemia and hypercholesterolemia;
- *Seloken/Toprol-XL* (metoprolol succinate), for the treatment of hypertension, heart failure and angina; and
- *Atacand* (candesartan cilexetil), for the treatment of hypertension and symptomatic heart failure.

AstraZeneca has adopted a unique CVRM strategy which includes investing in rigorous clinical programmes evaluating the use of its medicines in large patient populations in both US, Europe and Established Rest of World markets ("**Established Markets**") and Emerging Markets. These trials include ambitious global randomised clinical trials that are as close as possible to clinical practice, as well as transformational real-world evidence ("**RWE**") research.

Randomised clinical trials

More than 60,000 patients are currently participating in AstraZeneca's R&D-led CV trials at more than 6,000 sites worldwide. AstraZeneca's focus on diabetes research includes almost 50 clinical trials worldwide, with an enrolment target of 56,000 patients. These randomised clinical trials include the DapaCare Programme, OLYMPUS and ROCKIES, and THEMIS.

Real-world evidence data

AstraZeneca's RWE studies include CVD-REAL and PRACTICAL, which both set out to deliver innovative data from large-scale settings.

Respiratory Medicines

AstraZeneca's key marketed respiratory products include: *Symbicort* (budesonide/formoterol) for the treatment of asthma and chronic obstructive pulmonary disease ("**COPD**"); *Pulmicort* (budesonide), a corticosteroid used for maintenance treatment of asthma; *Duaklir* (aclidinium/formoterol), a dual bronchodilator intended for maintenance symptom control in COPD patients; *Tudorza/Eklira* (aclidinium), a treatment for symptomatic mild to moderate COPD patients in need of maintenance therapy; *Bevespi Aerosphere* (glycopyrrolate and formoterol fumarate), for the long-term maintenance treatment of airflow obstruction in COPD patients, including chronic bronchitis and/or emphysema; *Daliresp/Daxas* (roflumilast), an oral phosphodiesterase-4 inhibitor for adults with severe COPD to decrease their number of exacerbations; and *Fasenra* (benralizumab), approved in November 2017 in the US, for patients with severe asthma with an eosinophilic phenotype and is a respiratory biologic with an eight-week maintenance dosing regimen.

Infection medicines

AstraZeneca's key marketed infection products include: *Synagis* (palivizumab), a humanised monoclonal antibody used for the prevention of serious lower respiratory tract disease; and *FluMist Quadrivalent/Fluenz Tetra* (influenza vaccine), an intra-nasal, live, attenuated, quadrivalent influenza vaccine.

In November 2018, AstraZeneca announced the divestment of *Synagis*' US rights to Swedish Orphan Biovitrum AB. ("**Sobi**"). Sobi will commercialise *Synagis* in the US and around 130 AstraZeneca employees will transfer to Sobi as part of the transaction. Sobi also has the right to participate in payments from the US profits and losses for MEDI8897, an extended half-life respiratory syncytial virus monoclonal antibody being investigated for the prevention of lower respiratory tract infections caused by respiratory syncytial virus in infants and young children.

Neuroscience medicines

AstraZeneca's key marketed neuroscience products include: *Vimovo* (naproxen/esomeprazole magnesium), a delayed release tablet generally approved for symptomatic relief in the treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis; *Movantik/Moventig* (naloxegol), a once-daily, peripherally-acting mu-opioid receptor antagonist approved for the treatment of opioid-induced constipation in adult patients; and *Seroquel IR/Seroquel XR* (quetiapine fumarate), for the treatment of schizophrenia and bipolar disease.

In May 2018, AstraZeneca announced an agreement with Luye Pharma Group, Ltd. for the sale and licence of the rights to *Seroquel IR* and *Seroquel XR* in the UK, China and other international markets. AstraZeneca had previously partnered the rights to *Seroquel IR* and *Seroquel XR* in Japan and Venezuela under prior agreements. *Seroquel*, used primarily to treat schizophrenia and bipolar disease, has lost its compound patent protection globally. The *Seroquel XR* formulation patents have now also expired in the majority of markets.

Gastrointestinal medicines

AstraZeneca's key marketed gastrointestinal products include: *Nexium* (esomeprazole), the first proton pump inhibitor ("**PPI**") for the treatment of acid-related diseases to offer clinical improvements over other PPIs and other treatments; and *Losec/Prilosec* (omeprazole), used for the short-term and long-term treatment of acid-related diseases.

In October 2018, AstraZeneca announced that it had entered into an agreement selling the rights to *Nexium* in Europe and *Vimovo* worldwide (excluding the US) to Grünenthal Group.

In January 2019, Ironwood Pharmaceuticals, Inc ("**Ironwood**") announced they had received marketing authorisation from the National Medical Products Administration in China for *Linzess* for the treatment of patients with irritable bowel syndrome with constipation. AstraZeneca entered into a collaboration in China with Ironwood in 2012.

Business Environment

Global pharmaceutical sales grew by 4.4 per cent. in 2018 to US\$982 billion (Source: IQVIA Solutions HQ Limited ("IQVIA"), IQVIA Midas Quantum Q3 2017 (including US data)). Established Markets saw an average revenue increase of 3.9 per cent and Emerging Markets revenue grew at 6.4 per cent. The US, China, Japan, Germany and France are the world's top five pharmaceutical markets by 2018 sales. In 2018, the US had 47.2 per cent. of global sales (2017: 47.2 per cent) (Source: IQVIA, IQVIA Midas Quantum Q3 2017 (including US data)).

The growth drivers

Increasing burden of chronic diseases

An ageing population and changes in society are contributing to steady increases in non-communicable diseases ("NCDs") with developing countries particularly affected as their populations grow. As the burden of NCDs grows, so do public expectations while governments' ability to meet them is constrained as finances are under stress. Low- and middle-income countries are also disproportionately affected by issues such as air pollution and climate change, thereby exacerbating social, economic and demographic inequalities. The World Health Organisation (the "WHO") estimates that NCDs kill 41 million people each year and disproportionately affect low- and middle-income countries where more than three quarters of these deaths occur.

Growing and ageing populations, increasing urbanisation

Patient populations are expanding. For example, the WHO continues to estimate that, by 2050, the world's population aged 60 years and older is expected to total some two billion, up from 900 million in 2015 and that, by then, 80 per cent. of all older people will live in low- and middle-income countries.

The world's population is rising and more people are living in cities, with an estimated three million people a week moving to cities in 2015. Urbanisation presents opportunities, such as greater wealth and access to better healthcare, but also new hazards and healthcare challenges, such as an increase in the prevalence of NCDs. These diseases include cancer and cardiovascular, metabolic and respiratory diseases which are often associated with urban lifestyle choices, including smoking, diet and lack of exercise. NCDs are also associated with ageing and, with the majority of the world's workforce rapidly ageing, healthcare costs are rising as people are living longer. In many markets, ageing populations mean the size of the labour force will stagnate or decline, resulting in a potential shortage of labour compared with the abundance of labour that has fuelled growth since the 1970s.

Advances in science and technology

Scientific innovation is critical to addressing unmet medical need. The delivery of new medicines will rely on a more advanced understanding of the underlying biology of the disease, and the use of new technology and approaches. These include genomics and digital healthcare. Scientific and technological breakthroughs in small molecules and in biologics are also helping accelerate innovation. Innovation will be accelerated through the use of large volumes of biological data from disease biology and genomics which is driving precision medicine, while advances in data management and data integration are improving the speed and quality of clinical trial processes. Such advances have resulted in increased numbers of FDA priority reviews and breakthrough designations.

The challenges

R&D productivity

The cost of developing new medicines continues to rise with annual global R&D investment estimated to be between US\$150 and US\$160 billion in 2018. Regulators and payers are demanding greater evidence of the comparative effectiveness of medicines. On the other hand, a greater emphasis on proof of concept is helping to improve productivity and reduce costs by showing the potential efficacy of drugs earlier in the development process. Against this background, the FDA approved 59 novel drugs in 2018 compared with 46 in 2017 and 22 in 2016. Nevertheless, the risk of any products failing at the development or launch stages, or not securing regulatory approvals continues.

Regulatory requirements

The public's expectation of safe, effective and high-quality medicines is reflected in a highly regulated biopharmaceutical industry. At the same time, AstraZeneca is seeing instances of government policy and regulation being introduced to stimulate innovation in drug development, and of regulatory health authorities implementing programmes intended to speed up patient access to transformative medicines. Examples of this include the 21st Century Cures Act of 2016 and the FDA Reauthorization Act of 2017 in the US, a new conditional early approval system in Japan and proposed changes to regulations in China.

In addition, international harmonisation of regulatory requirements is being advanced in many areas through organisations such as the International Council for Harmonization, the Pharmaceutical Inspection Cooperation Scheme, the Pan American Network for Drug Regulatory Harmonization, and the International Conference of Drug Regulatory Authorities.

There are also uncertainties. In Europe, they include how the UK will work with the EU regulatory system following its planned exit from the EU and the approach the UK will take to establishing its own regulatory system outside the EU (and the likely disruption this will cause to regulatory processes).

The implementation of the EU Clinical Trials Regulation has also been delayed. Nevertheless, paediatrics and use of digital tools in clinical development, as well as patients' access to innovative medicines and stakeholders interactions to improve drug development, are high on the EU agenda.

In biosimilar development, regulatory requirements for the registration of biosimilar products are becoming better defined. However, significant areas of regulatory policy are still evolving. Among these are transparency of data regarding the level of evidence to support approval of claims for biosimilarity in labelling, standards for interchangeability and pharmaceutical substitution, and traceability of pharmacovigilance reports through naming conventions that permit differentiation of products.

Increased transparency of data used for regulatory decision making continues to be an area of interest to regulatory authorities in the EU and the US. It has recently attracted interest elsewhere, such as in Canada. AstraZeneca believes that transparency enhances the scientific understanding of how its medicines work and is in the medical interest of its patients.

Pricing of medicines

Pricing and reimbursement remain challenging in many markets. AstraZeneca continues to see examples where healthcare services (including pharmaceuticals) are highly regulated by governments, insurers and other private payers through various controls on pricing and reimbursement. Implementation of cost-containment reforms and shifting market dynamics are further constraining healthcare providers, while difficult economic conditions burden patients who have out-of-pocket expenses relating to their medicines. Pharmaceutical companies are now expending significant resources to demonstrate the economic as well as the therapeutic value of their medicines.

The need and desire for payers to manage drug expenditure has been heightened by the shift over the last decade from a primary care to a specialty care focus. Specialty drugs are used for the treatment of complex, chronic or rare conditions such as cancers, and pricing for these products reflects the higher value they bring to patients and payers, as well as the smaller patient numbers as a result of targeted treatment options.

Pricing controls and transparency measures remain a priority in key markets such as China, where the National Reimbursement Drug List ("NRDL") was updated in 2017. In Europe, governments continue to implement and expand price control measures for medicines, and the EU has committed to introducing a harmonised health technology assessment review. In other markets, there has been a trend towards rigorous and consistent application of pricing regulations, including reference pricing and group/alliance purchasing.

There is also pressure on pricing in the US. For example, federal and state policymakers are considering legislative and regulatory efforts to lower drug prices and to implement transparency measures. While legislative efforts to repeal and replace the Affordable Care Act ("ACA") have not been successful, the current administration and members of Congress remain focused on healthcare policy priorities, including efforts to increase competition and generic drug use in government programmes which would create downward pressure on pricing. The healthcare industry may also be used as a means to offset government spending. US federal agencies continue to propose and implement policies and programmes with the goal of reducing costs, increasing transparency, transforming the delivery system, and improving quality and patient outcomes.

Loss of exclusivity and genericisation

Patent protection for pharmaceutical products is finite and, after protection expires, payers, physicians and patients gain greater access to generic alternatives (both substitutable and analogue) in many important drug classes. These generic alternatives are primarily lower priced because generic manufacturers are largely spared the costs of R&D and market development. As a result, demand for generics is high. For prescriptions dispensed in the US in 2018, generics constituted 84.8 per cent. of the market by volume (2017: 84.9 per cent.).

Generic competition can also result from patent disputes or challenges before patent expiry. Increasingly, generics companies are launching products 'at risk', for example, before resolution of the relevant patent litigation. This trend, which is likely to continue, creates significant market presence for the generic version while the litigation remains unresolved. Given the unpredictable nature of patent litigation, some companies have settled such challenges on terms acceptable to the innovator and generic manufacturer. While competition authorities generally accept such agreements as a legitimate way to settle these disputes, they have questioned some settlements as being anti-competitive.

Biologics typically retain exclusivity for longer than traditional small molecule pharmaceuticals, with less generic competition. With limited experience to date, the substitution of biosimilars for the original branded product has not followed the same pattern as generic substitution in small molecule products and, as a result, erosion of the original biologic's branded market share has not been as rapid. This is due to biologics' complex manufacturing processes and the inherent difficulties in producing a biosimilar, which could require additional clinical trials. However, with regulatory authorities in Europe and the US continuing to implement abbreviated approval pathways for biosimilar versions, innovative biologics are likely to face increased competition. Like biologics, some small molecule pharmaceutical products are in complex formulations and/or require technically challenging manufacturing and thus may not follow the pattern of generic market erosion seen with traditional, tableted pharmaceuticals. For those products, the introduction of generic alternatives (both substitutable and analogue) can be slower.

Trust

The pharmaceutical industry continues to face challenges in building and maintaining its reputation and the trust of its stakeholders. This reflects past sales and marketing practices, pricing practices by some, as well as legal disputes between pharmaceutical companies and governmental and regulatory authorities.

Companies, including those in the pharmaceutical industry, have been investigated by the China Public Security Bureau following allegations of bribery, and criminal and financial penalties have been imposed. In the US, investigations by the US Department of Justice and the Securities and Exchange Commission under the US Foreign Corrupt Practices Act continue, as do investigations by the UK Serious Fraud Office under the UK Bribery Act.

To address these challenges, companies are seeking to: (i) embed a culture of ethics and integrity; (ii) adopt higher governance standards; (iii) promote sustainability programmes, particularly focused on access to healthcare; and (iv) improve relationships with employees, shareholders and other stakeholders. Companies are also adopting more 'patient-centric' approaches that go 'beyond the pill' to encompass all aspects of disease management – prevention, screening, diagnosis, treatment and rehabilitation.

Strategy

AstraZeneca announced its strategy in March 2013, outlining plans to:

1. Achieve Scientific Leadership
2. Return to Growth
3. Be a Great Place to Work

The first phase was focused on rebuilding its pipeline. As part of the second phase AstraZeneca drove its Growth Platforms forward, continued to launch new medicines and made them available to patients. In 2018, AstraZeneca returned to Product Sales growth. Following the progress made, AstraZeneca updated its three strategic objectives in February 2019 to the following three strategic pillars:

1. Deliver growth and therapy area ("TA") leadership
2. Accelerate innovative science
3. Be a great place to work

1. *Deliver growth and TA leadership*

This pillar focuses on delivering the potential of already-developed medicines and aims to ensure that AstraZeneca is in a leadership position in each of its main TAs by 2025 by:

- Driving growth and profitability – AstraZeneca has developed a number of leading medicines and, having returned to Product Sales growth in 2018, believes it can now seek to maximise their full potential, building a sustainable company and driving profitability so that it can continue to invest in the future.
- Impacting and improving the whole patient journey – AstraZeneca seeks to become more patient-centric and improve the whole patient experience, from disease prevention and screening, diagnosis and treatment through to rehabilitation.
- Leading in outcomes-based payer models – AstraZeneca aims to lead in the use of new value-based payer models and real-world evidence, and play its part in managing the totality of healthcare costs.

2. *Accelerate innovative science*

The second strategic pillar focuses on how AstraZeneca can bring through the next wave of innovation from its industry-leading pipeline by:

- Pulling through projects from its mid-stage pipeline to late-stage so that it is continually moving through potential medicines to launch.
- Maintaining its scientific edge by entering and advancing its work in new areas of science to deliver the next wave of medicines, including the next wave of disruptive biology.
- Accelerating its efforts in artificial intelligence, data and digital to support its efforts and the advancement of its science and medicines.

3. *Be a great place to work*

This pillar is carried forward from the 2013 strategy and AstraZeneca believes that there is always room to improve further by:

- Making a bigger difference to the societies in which it operates, particularly in relation to access to its medicines, impact on the environment and advancing the policy landscape.
- Advancing its culture, and ensuring it builds and adapts its capabilities to support its continued success.

Organisation

AstraZeneca's operating model includes its R&D, Operations and Commercial functions, together with its Enabling Units.

In January 2019, AstraZeneca announced organisational changes to support continued scientific innovation and commercial success as it enters the next phase in its strategic development. The changes are designed to further integrate R&D and accelerate decision making and the launches of new medicines.

AstraZeneca is also enhancing its commercial functions to increase collaboration with its R&D organisation, enabling greater commitment to its main therapy areas.

The functions will share many common areas, including basic biology and science platforms as well as medicine supply, manufacturing and IT infrastructure to improve efficiency. These resources will continue to be allocated on a Group-wide basis, according to the overall therapy-area considerations and strategy. Since 2007, AstraZeneca has made significant efforts to restructure and reshape its business to control costs and improve long-term competitiveness.

R&D

AstraZeneca has three strategic R&D centres: Gaithersburg, Maryland, US, Gothenburg, Sweden and Cambridge, UK.

In January 2019, AstraZeneca created therapy area-focused R&D organisations that are responsible for discovery through to late-stage development – one for BioPharmaceuticals (CVRM and Respiratory) and one for Oncology. This is designed to enable it to "follow the science" by accelerating promising early-stage assets and life-cycle management programmes, as well as providing new opportunities for combinations.

Operations

AstraZeneca's Operations function plays a key role in development, manufacturing, testing and delivery of its medicines to its customers.

Commercial

In 2018, AstraZeneca's sales and marketing functions were grouped into regions: North America (US and Canada); Europe; and International (Emerging Markets, including China, and Australia and New Zealand). Japan is categorised separately and is one of AstraZeneca's Growth Platforms (as defined below).

In January 2019, AstraZeneca created two commercial units – one for BioPharmaceuticals and one for Oncology. The creation of the BioPharmaceuticals commercial unit aligns product strategy, previously undertaken by its Global Product and Portfolio Strategy group, and commercial delivery across CVRM and Respiratory in the US and Europe. These responsibilities mirror the Oncology Business Unit, formed in April 2017, and sharpen its focus on its main therapy areas as it brings new medicines to patients. The International commercial organisation remains unchanged.

Restructuring

Since 2007, AstraZeneca has undertaken significant efforts to restructure and reshape its business to improve its long-term competitiveness. The first phases of this restructuring, involving the integration of MedImmune, efficiencies within the R&D function and a reduction in selling, general and administrative costs, were completed in 2011. The targeted commercial restructuring announced in 2015 has also been successfully completed with a total cost of US\$151 million.

In 2016, AstraZeneca announced plans to advance its strategy through sharper focus by streamlining operations, primarily in Commercial and Manufacturing, to redeploy investment to key therapy areas, particularly Oncology. Restructuring costs associated with this programme were initially forecast to be US\$1.5 billion by the end of 2017 and generate net annualised benefits of US\$1.1 billion by 2018. The total cost estimate is now US\$1.3 billion to be incurred by the end of 2019, with benefits expected to be US\$1.1 billion in 2019.

In addition to the 2016 plan, there are two further active programmes. The first is the continuation of the Phase 3 restructuring that was announced in 2012, superseded by Phase 4 in 2013 and subsequently expanded in 2014. This initiative consists of centralisation of AstraZeneca's global R&D footprint into three strategic centres, transformation of the IT organisation, closure of a number of manufacturing facilities and other activities to simplify and streamline the organisation. At the time of the announcement, the Phase 4 programme was estimated to incur US\$3.2 billion of costs and deliver US\$1.1 billion of annualised benefits by 2016. By the end of 2018, the Phase 4 programme had incurred costs of US\$3.5 billion, creating headroom for investment in AstraZeneca's pipeline and launch capability. The Phase 4 programme is now expected to complete in 2021 with total programme costs estimated to be US\$3.7 billion and annualised benefits of US\$1.2 billion.

The second step was initiated in 2016 and relates to multi-year transformation programmes within AstraZeneca's General & Administrative functions (principally finance and human resources). AstraZeneca expects these transformation programmes to deliver annualised benefits of US\$100 million by 2019. By the end of 2018, these programmes had incurred costs of US\$304 million with total expected costs rising to US\$376 million.

The aggregate restructuring charge incurred in 2018 across all AstraZeneca's restructuring programmes was US\$697 million (2017: US\$807 million), including the US biologics site closures at Longmont and Boulder,

Colorado, and other acquired assets. Final estimates for programme costs, benefits and headcount impact in all functions are subject to completion of the requisite consultation in the various areas.

Sustainability

AstraZeneca is committed to operating in a way that recognises the interconnection between business growth, the needs of society and the limitations of the planet. This means delivering AstraZeneca's business strategy in a way that broadens access to its medicines, minimises the environmental footprint of its products and processes, and ensures that ethics and transparency underpin everything it does.

Sustainability strategy

AstraZeneca's sustainability strategy is aligned with its purpose and business strategy, allowing it to maximise the benefit for its patients, its business, broader society and the planet. In 2018, a structured sustainability materiality assessment that engaged external and internal stakeholders reaffirmed AstraZeneca's direction and refined the priority areas. AstraZeneca measures its progress through annual and long-term targets.

1. *Broadening access to healthcare*

AstraZeneca aims to improve lives by increasing access to healthcare. It has identified the following priority areas: (i) disease prevention and treatment; (ii) affordability; (iii) investments in health systems; (iv) responsible R&D and (v) the environment's impact on health.

2. *Furthering ethics and transparency*

AstraZeneca has committed to furthering ethics and transparency in everything it does. It has identified the following priority areas: (i) ethical business culture; (ii) inclusion & diversity; (iii) talent & workforce evolution; (iv) workforce wellbeing and safety; (v) responsible supply chain; and (vi) human rights.

3. *Protecting the environment*

AstraZeneca strives to reduce environmental impacts on human health and the natural world. It has identified the following priority areas: (i) greenhouse gas emissions; (ii) waste; (iii) water; (iv) product environmental stewardship and (v) pharmaceuticals in the environment.

Protecting the environment

AstraZeneca 'follows the science' to protect the planet by managing its impact on the environment across all its operations. AstraZeneca's Code of Ethics is the overarching document for its environmental management system. It applies to all functions and locations and is supported by global standards and procedures that establish mandatory requirements in key risk areas. AstraZeneca monitors and manages performance through comprehensive assurance programmes that include performance reporting, internal auditing and an annual management review. AstraZeneca is on track to deliver its 2016 to 2025 environment targets.

AstraZeneca's 2018 targets (against a 2015 baseline) included: (i) reducing its operational greenhouse gas footprint in line with its approved Science Based Target; (ii) limiting the increase in its energy consumption to no more than 2 per cent. to 1,841 GWh; (iii) limiting the increase in its waste generation to less than 7 per cent. to 32,811 tonnes; and (iv) reducing water use by 7 per cent to 4.03 million m³.

To support the achievement of AstraZeneca's targets, a resource efficiency capital fund has been in place since 2015 to invest in projects at sites. In 2018, approximately US\$19 million (2017: US\$19 million) was committed to resource efficiency projects at AstraZeneca's manufacturing and R&D sites, and a further US\$15 million has been committed for 2019.

Business Review

Achieve scientific leadership

AstraZeneca is using its distinctive scientific capabilities, as well as investing in key programmes and focused business development, to deliver life-changing medicines.

During 2018, AstraZeneca was involved with:

- 23 approvals of new molecular entities ("NMEs") or major life-cycle management ("LCM") projects in major markets:
 - 13 oncology approvals for *Imfinzi*, *Lumoxiti*, *Lynparza* and *Tagrisso*
 - six CVRM approvals for Bydureon, Bydureon BCise, Lokelma and roxadustat
 - three respiratory approvals for *Bevespi* and *Fasenra*
 - one other approval for *Nexium*
- 28 NME or major LCM regulatory submissions in major markets
- 19 Phase III NME investment decisions
- nine Phase II starts
- Accelerated reviews including:
 - one Breakthrough Therapy Designation
 - three Orphan Drug Designations
 - three Priority Review Designations
- 18 projects discontinued

Scientific leadership and collaboration

One of the measures of AstraZeneca's success in achieving scientific leadership and demonstrating the quality of research conducted in its laboratories is the number of publications in high-quality and 'high-impact' journals. It is also critical for recruiting and retaining the best scientists from around the world. Scientists from AstraZeneca's R&D organisations have published 102 manuscripts (up by 20 compared with 2017, a record number) in 'high-impact' peer-reviewed journals, each with an impact factor exceeding 15 (Thomson Reuters 5yr IF score) and a score exceeding 955 in total. This represents a fourteen-fold improvement since 2012.

Early science

During 2018, AstraZeneca's R&D organisations worked to strengthen AstraZeneca's early-stage product portfolio by exploring novel biology across its disease areas and developing the best molecules to address unmet medical need. The diversity and technologies applied in AstraZeneca's early pipeline is exemplified by the increased number of new modalities entering clinical development: 12 in 2018 compared to six in 2012. For example, AstraZeneca's collaboration with Moderna Therapeutics is exploring the use of modified ribonucleic acid ("**mRNA**") for cardiac regeneration in patients undergoing coronary artery bypass graft surgery as well as an additional programme where AstraZeneca are evaluating anti-cancer T-cell responses with mRNA therapies in patients with solid tumours. With Ionis Pharmaceuticalls, Inc., AstraZeneca is investigating an antisense oligonucleotide in immuno-oncology (*danvatersin*), in combination with *Imfinzi*. With Pieris Pharmaceuticals, AZD1402 entered clinical development in 2018 as a novel inhaled drug for asthma based on its 'proprietary bicyclic peptide product platforms. In addition, AstraZeneca continues to evaluate its DNA-based cancer vaccine targeting HPV-16 and HPV-18 in collaboration with Inovio Pharmaceuticals, Inc.

Since 2014, AstraZeneca has had 26 diagnostic tests approved in the US, EU and Japan. They support four precision medicines for patients with some of the most challenging diseases of current times, including three for lung and ovarian cancers: therapies that target the EGFR, including the T790M resistance mutation; the poly ADP ribose polymerase pathway; and the programmed death-ligand pathway. Approximately 90 per cent. of AstraZeneca's pipeline now has a precision medicine approach and reflects the broad range of cutting-edge technologies, tissue diagnostics, next-generation sequencing and point of care diagnostics that it has introduced.

Transforming medical science

AstraZeneca is determined to advance its understanding of disease biology to uncover novel drivers for the diseases it aims to treat, prevent, and even cure. AstraZeneca aims to foster an environment where its scientists can freely share their ideas and collaborate with the best external partners. Management believe that AstraZeneca's approach to science is exemplified by the number of joint research facilities it has established with leading scientific centres, such as the Karolinska Institutet in Sweden and the Cancer Research UK, Cancer Institute in the UK. In 2018, AstraZeneca extended its joint research facility at the Max Planck Institute to include the Chemical Genomics Centre III, focused on novel basic research in the biosciences and chemical biology. With the Swedish Innovation Bridge Company, AstraZeneca established a partnership with Procella Therapeutics and Smartwise to develop novel stem cell-based therapies for heart failure. The Blue-Sky fund AstraZeneca established with the MRC Laboratory of Molecular Biology ("**LMB**") is now in its fourth year of funding projects which involve 40 per cent. of LMB's principal investigators. A recent project breakthrough uncovered the first protein structures for human ataxia telangiectasia mutated, a key trigger protein in the DNA damage response and a prime therapeutic target in cancer. In 2018, AstraZeneca announced a collaboration to develop and commercialise a gene therapeutic for patients with chronic lung disease, utilising 4D Molecular Therapeutics novel discovery platform to generate optimised adeno associated virus vectors. AstraZeneca also continues to advance its strategic research collaboration with Ethris GmbH where it is evaluating mRNA-based therapies in pulmonary diseases.

Innovating in drug discovery

AstraZeneca is exploring emerging technologies to accelerate the design and testing of tomorrow's medicines. Its teams are also looking across the discovery and development process, to understand where it can harness new technologies and further automate processes. In drug discovery, AstraZeneca's teams are facilitating rapid, unbiased drug design and speeding up compound synthesis through improvements in AI algorithmic processes. In the previous two years, AstraZeneca's scientists have published more than 20 scientific publications showing improvements in algorithmic processes in drug design. AstraZeneca is also collaborating with the University of Bern and University of Bonn, on a European Commission-funded project that harvests the power of supercomputers to speed up drug discovery using machine learning. Through the acquisition of Definiens in 2014, AstraZeneca is developing new AI approaches to evaluate complex morphology, such as in the tumour microenvironment. In early development, AstraZeneca is starting to connect high-density datasets, from imaging, biosensors, multiomics and quality-of-life information, to inform earlier decision making in clinical trials. In a recent publication in *Lancet Respiratory Medicine*, AstraZeneca describes a novel modelling tool that has the potential to reduce the time of Phase II trials in respiratory by half.

Late-stage development

During 2018, AstraZeneca's R&D organisation delivered clinical trial data and submissions that resulted in 23 approvals for new medicines in the US, EU, China and Japan. AstraZeneca's pipeline includes 149 projects, of which 131 are in the clinical phase of development, and it is making significant progress in advancing its late-stage programmes through regulatory approval with 28 NME or major LCM regulatory submissions during 2018.

At the end of the year, AstraZeneca had eight NME projects in pivotal studies or under regulatory review (covering 15 indications), compared with 11 at the end of 2017.

Also in 2018, 20 NMEs progressed to their next phase of development and 18 projects were discontinued: 15 for poorer than anticipated safety and efficacy results; and three as a result of a strategic shift in the environment or portfolio prioritisation.

As is to be expected when AstraZeneca is investigating treatments for diseases that are hard to treat, it also had some setbacks during the year. These included disappointing Phase III data results. For example, the results of the MYSTIC trial showed that *Imfinzi* in combination with *tremelimumab* for 1st line NSCLC did not meet the primary endpoint of overall survival ("**OS**") and the Phase III EAGLE trial of *Imfinzi* and *tremelimumab* did not meet the primary endpoints of improving OS in advanced head and neck cancer relative to standard of care chemotherapy. Along with Lilly, AstraZeneca also discontinued development of lanabecestat for Alzheimer's disease after an independent data monitoring committee concluded that the trials were unlikely to meet their primary endpoints and recommended the trials be stopped for futility.

Accelerating the pipeline

AstraZeneca's R&D organisations are prioritising its investment in specific programmes to accelerate them so that new treatments get to patients more quickly but still safely. As a result, AstraZeneca had numerous study read-outs in 2018, including *Lynparza* in 1st line BRCA-mutated advanced ovarian cancer, *Imfinzi* OS results in unresectable stage 3 NSCLC, the Farxiga cardiovascular outcomes trial in adults with type-2 diabetes and the *Fasenra* Phase III extension trial evaluating long-term safety and efficacy. AstraZeneca's teams have also been quick to turn positive clinical trial data into regulatory submissions. In 2018, AstraZeneca made submissions in the US, EU, Japan and China for *Lynparza* for 1st line maintenance treatment for advanced BRCA-mutated ovarian cancer, and *Bevespi* for COPD in the EU, Japan and China. AstraZeneca also received approval in the US and EU for *Lokelma* for the treatment of adults with hyperkalaemia, *Lumoxiti* in the US for the treatment of adults with relapsed or refractory HCL, *roxadustat* for the treatment of anaemia in Chronic Kidney Disease in China, *Fasenra* for severe asthma in the EU and Japan, and US approval for *Lynparza* for 1st line maintenance treatment for advanced BRCA-mutated ovarian cancer.

In 2018, AstraZeneca presented scientific rationale that resulted in four regulatory designations for Breakthrough Therapy or Priority Review for new medicines which offer the potential to address unmet medical need in certain diseases, including *tezepelumab* in patients with severe asthma, *Lynparza* for ovarian cancer, *Tagrisso* in 1st line EGFR mutated NSCLC and *Lumoxiti* in 3rd line HCL. AstraZeneca also secured Orphan Drug designation for the development of three medicines to treat very rare diseases including *Lynparza* for treatment of pancreatic cancer, *selumetinib* for the treatment of neurofibromatosis type 1 and *Fasenra* for the treatment of eosinophilic granulomatosis with polyangitis.

AstraZeneca also collaborates to advance its clinical research – from strategic alliances with contract research organisations for the delivery of clinical trials, to academic collaborations.

Return to growth

AstraZeneca is focusing on its growth platforms which consist of Emerging Markets, Respiratory, New CVRM, Japan and Oncology ("**Growth Platforms**"), and transforming the business through specialty care, devices and biologics. AstraZeneca's return to product sales growth was underpinned by its focus on Growth Platforms and leveraging its strong global commercial presence, particularly in Emerging Markets, to ensure the right medicines are available and that patients have access to them.

AstraZeneca's plans for growth

AstraZeneca's Commercial teams, which comprised around 36,100 employees at the end of 2018, are active in more than 100 countries. In most countries, AstraZeneca sells its medicines through wholly-owned local marketing companies. AstraZeneca also sells through distributors and local representative offices. It markets its products largely to primary care and specialty care physicians.

AstraZeneca's return to product sales growth was underpinned by its Growth Platforms. These comprise AstraZeneca's three main therapy areas, together with Emerging Markets and Japan. In 2018 they grew by 13 per cent. (12 per cent at constant exchange rate ("**CER**")) and represent 84 per cent. of total revenue.

Sales of *Tagrisso*, *Imfinzi*, *Lynparza*, *Calquence*, *Lumoxiti*, *Brilinta*, *Farxiga*, *Lokelma*, *Bevespi* and *Fasenra* (together, "**New Medicines**") generated incremental sales of US\$2.8 billion at CER and represented 30 per cent. of total revenue. These new medicines are important platforms for future growth. In Emerging Markets, they represented 15 per cent. of sales, up from 10 per cent. in 2017 and, in the US, they represented 48 per cent. of product sales, up from 26 per cent. US performance reflected, in particular, the success of the new Oncology medicines plus the strong performance of *Fasenra*. In Europe, the decline in product sales reflected the impact of generic *Crestor* medicines in various markets in 2017 and continued competitive and price pressures. New Medicines represented 28 per cent. of product sales, up from 18 per cent. in 2017. In Established Rest of World, New Medicines represented 24 per cent. of sales in the year, up from 13 per cent. in 2017. However, the pharmaceutical market is highly competitive. For example, AstraZeneca's diabetes franchise continues to see pricing pressure. In immuno-oncology, the large number of clinical trials that are being carried out highlight the competitive nature of this area and renders speed to market critical.

Pricing and delivering value

AstraZeneca's medicines help treat unmet medical need, improve health and create economic benefits. Effective treatments can lower healthcare costs by reducing the need for more expensive care, preventing more

serious and costly diseases and increasing productivity. AstraZeneca is committed to a pricing policy for its medicines based on four principles: (i) AstraZeneca determines the price of its medicines while considering their full value for patients, payers and society and the agreement on price involves many national, regional and local stakeholders, reflecting factors such as clinical benefit, cost effectiveness, improvement to life expectancy and quality of life; (ii) AstraZeneca aims to ensure the sustainability of both the healthcare system and its research-led business model and it believes that it shares a collective responsibility with healthcare providers and other stakeholders to work together to enable an efficient healthcare system for patients today and support a pipeline of new medicines for patients tomorrow; (iii) AstraZeneca seeks to ensure appropriate patient access to its medicines and works closely with payers and providers to understand their priorities and requirements, and plays a leading role in projects to align better the requirements of regulatory and health technology assessment agencies or other organisations that provide value assessment of medicines: for example, it has a leading role in the European IMI ADAPT-SMART programme for exploring adaptive licensing; and (iv) AstraZeneca pursues a flexible pricing approach that reflects the wide variation in global healthcare systems and it has developed patient access programmes that are aligned with the ability to pay of patients and healthcare systems and AstraZeneca is committed to the appropriate use of managed entry schemes and the development of real-world evidence and it is investigating innovative approaches to the pricing of medicines, such as payment for outcomes received by the patient and healthcare system.

US

As the sixteenth largest prescription-based pharmaceutical company in the US, AstraZeneca has a 2.5 per cent market share of US pharmaceuticals by sales value. In 2018, product sales in the US increased by 11 per cent. to US\$6,876 million (2017: US\$6,169 million).

The US healthcare system is complex with multiple payers and intermediaries exerting pressure on patient access to branded medicines through regulatory and voluntary rebates. Regulatory rebates are statutorily mandated chargebacks and discounts paid on government-funded programmes such as Medicaid, Department of Defence (including TRICARE) and Department of Veteran's Affairs. Voluntary rebates are paid to managed care organisations and pharmacy benefit managers for commercially insured patients, including Medicare Part D patients. In the Medicare Part D programme, in addition to voluntary negotiated rebates, branded pharmaceutical manufacturers are statutorily required to pay a percentage of the patient's out-of-pocket costs during the 'coverage gap' portion of their benefit design. From the beginning of 2019, the mandatory coverage gap discount increased to 70 per cent. from its former 50 per cent., as a result of the passage of legislation in 2018. As part of the ACA, AstraZeneca also pays a portion of an overall industry Patient Protection and Affordable Care Act Branded Prescription Drug Fee.

In 2018, the overall measurable reduction in AstraZeneca's profit before tax for the year due to discounts on branded pharmaceuticals in the Medicare Part D Coverage Gap and an industry-wide HealthCare Reform Fee was US\$432 million (2017: US\$119 million).

In the US, there is significant pricing pressure driven by payer consolidation, restrictive reimbursement policies and cost control tools, such as exclusionary formularies and price protection clauses. Many formularies, which specify particular medicines that are approved to be prescribed in a healthcare system, or under a health insurance policy, employ 'generic first' strategies and/or require physicians to obtain prior approval for the use of a branded medicine where a generic alternative exists. These mechanisms can be used by intermediaries to limit the use of branded products and put pressure on manufacturers to reduce net prices. In 2018, 84.8 per cent. of prescriptions dispensed in the US were generic, compared with 84.9 per cent. in 2017. In addition, patients are seeing changes in the design of their health plan benefits and may experience variation, including increases, in both premiums and out-of-pocket payments for their branded medications. The patient out-of-pocket spend is generally in the form of a co-payment or co-insurance, but there is a growing trend towards high deductible health plans which require patients to pay the full list price until they meet certain out-of-pocket thresholds.

Ongoing scrutiny of the US pharmaceutical industry, focused largely on pricing, has been the basis of multiple policy proposals in the US. In May 2018, the Trump administration issued its 'Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs', which included a wide range of policy proposals that would impact the US pharmaceutical industry if implemented. Proposed changes under consideration include, but are not limited to, fundamentally changing the role of rebates in the pharmaceutical supply chain, reforms to the 340B Drug Pricing Program, and policies to increase competition in the Medicare programme and encourage generic drug use. The Trump administration has already taken action on several of the policies discussed in the Blueprint, and more policy actions are pending. In addition, lawmakers at both the federal and state level have sought

increased drug pricing transparency and have proposed and implemented policies that include measures relating to the submission of proprietary manufacturer data, establishment of price parameters that are indexed to certain federal programmes, and reporting of changes in pricing beyond certain thresholds. Though widespread adoption of a broad national price control scheme in the near future is unlikely, AstraZeneca continues to comply with new state-level regulations in this area and it recognises the sustained potential for substantial changes to laws and regulations regarding drug pricing that could have a significant impact on the pharmaceutical industry.

AstraZeneca understands that its medicines will not benefit patients if they are unable to afford them and it offers a number of resources and programmes that can help increase patients' access to medication and reduce their out-of-pocket costs. AstraZeneca focuses its formulary access on affordability for patients through rebate payments as well as savings cards for eligible patients when the out-of-pocket costs are not affordable. AstraZeneca has one of the longest-standing patient assistance programmes in the industry, AZ&Me, which provides eligible patients with AstraZeneca's medicines at no cost. AstraZeneca has provided prescription savings to four million patients across the US and Puerto Rico over the past 10 years.

Europe

The total European pharmaceutical market was worth US\$196 billion in 2018. AstraZeneca is the fifteenth largest prescription-based pharmaceutical company in Europe with a 2.0 per cent. market share of pharmaceutical sales by value.

In 2018, AstraZeneca's product sales in Europe decreased by 6 per cent. at actual rate of exchange (10 per cent. at CER) to US\$4,459 million (2017: US\$4,753 million). Key drivers of the decline, leaving aside the impact of divestments such as *Seloken*, *Atacand*, *Nexium* and *Zomig*, were continued competition from *Symbicort* analogues, loss of exclusivity for *Crestor*, and the continued impact of early generic entry in certain markets for *Faslodex*, which AstraZeneca expects to continue in 2019. The continued macroeconomic environment, pricing pressure from payers and parallel trade across markets also affected sales. Despite these conditions, AstraZeneca continued to launch innovative medicines across Europe and saw encouraging performance for certain products across its Growth Platforms, in particular with *Forxiga*, *Brilinta*, *Fasenra*, *Lynparza* and *Tagrisso*. Oncology sales in Europe grew by 19 per cent. (14 per cent. at CER), partly driven by the approval of *Tagrisso* for the treatment of patients in the 1st line EGFR mutant setting in June 2018. *Lynparza* sales grew by 46 per cent. (41 per cent. at CER), partly benefiting from the approval in May 2018 for its use as a tablet based treatment for platinum-sensitive ovarian cancer, regardless of breast cancer status. *Brilique* sales growth of 18 per cent. (13 per cent. at CER) was accompanied by *Forxiga* sales growth of 30 per cent. (24 per cent. at CER). *Fasenra* was successfully launched in several European countries, with a strong initial uptake.

Established Rest of World

In 2018, product sales in Japan decreased by 9 per cent. at actual rate of exchange (11 per cent. at CER) to US\$2,004 million (2017: US\$2,208 million), as a result of the biennial government price cuts and increased intervention from the government to rapidly increase the volume share of generic products. In September 2017, a *Crestor* authorised generic entered the market and in December 2017 AstraZeneca saw more than 20 generic companies enter the Japanese statin market with generic rosuvastatin which has strongly impacted *Crestor* product sales with a decrease of 60 per cent. Leaving aside these generic restraints, Japan is presenting strong growth from the brands in AstraZeneca's Growth Platforms and *Nexium*. In addition, there were particularly strong performances from *Tagrisso*, *Fasenra*, *Imfinzi*, *Lynparza* and the Diabetes franchise. AstraZeneca now holds twelfth position in the ranking of pharmaceutical companies by sales of medicines in Japan. Japan remains an attractive market for innovative pharmaceuticals.

Canada has a mixed public/private payer system for medicines that is funded by the provinces, insurers and individual patients. It has also now become common for public payers to negotiate lower non-transparent prices after they have gone through a review by the Canadian Agency for Drugs and Technology in Health, a health technology assessment body. Most private insurers pay full price, although there is increasing pressure to achieve lower pricing. Overall, the split for AstraZeneca's portfolio is 62 per cent. funded by private payers and 38 per cent. by public plans.

AstraZeneca's sales in Australia and New Zealand declined by 16 per cent. at actual rate of exchange (14 per cent. at CER) in 2018. This was primarily due to the continued erosion of *Nexium* and *Seroquel* by generic medicines, further price reductions on established brands and entry of an analogue for *Symbicort* in Australia, which had an impact on both price and volume. Consequently, sales in 2018 declined at a greater rate compared

to that seen in 2017. However, the pace of generic erosion has moderated notably with *Crestor* and *Atacand*, while the sales growth from new products such as *Brilinta*, *Lynparza* and the Diabetes portfolio grew by 4 per cent. at actual rate of exchange (6 per cent. at CER), 41 per cent. at actual rate of exchange (43 per cent. at CER) and 4 per cent. at actual rate of exchange (6 per cent. at CER) respectively.

Emerging Markets

Emerging Markets comprise various countries with dynamic, growing economies. These countries represent a major growth opportunity for the pharmaceutical industry due to high unmet medical need and sound economic fundamentals. Emerging Markets are not immune, however, to economic downturn. Market volatility is higher than in Established Markets and various political and economic challenges exist. These include regulatory and government interventions. In selected markets, governments are encouraging local manufacturing by offering more favourable pricing legislation and pricing is increasingly controlled by governments with price referencing regulations.

Growth drivers for Emerging Markets include new medicines across AstraZeneca's Oncology, CVRM and Respiratory portfolios. To educate physicians about AstraZeneca's broad portfolio, it is selectively investing in sales capabilities where opportunities from unmet medical need exist. AstraZeneca is also expanding its reach through multi-channel marketing and external partnerships.

With revenues of US\$6,891 million, AstraZeneca was the fourth largest multinational pharmaceutical company, as measured by prescription sales, and the fastest-growing top 10 multinational pharmaceutical company in Emerging Markets in 2018.

China

In China, AstraZeneca is the second largest pharmaceutical company by value in the hospital sector, as measured by sales. Sales in China in 2018 increased by 28 per cent. at actual rate of exchange (25 per cent. at CER) to US\$3,795 million (2017: US\$2,955 million). AstraZeneca delivered sales growth above the growth rate of the hospital market sector through strategic brand investment, systematic organisational capability improvements and long-term channel expansion programmes in main therapy areas. In addition, *Tagrisso* was listed in the NRDL and AstraZeneca launched *Lynparza* during 2018. Pricing practices remain a priority for regulators, and new national regulations, in addition to provincial and hospital tenders, continue to put increasing pricing pressures on pharmaceutical companies in China. In addition, the planned roll-out of the Generics Quality Consistency Evaluation will have an impact on pharmaceuticals budgets and pricing through setting new standards for bioequivalence that generic products must adhere to. The outcome of the latest round of tenders involving *Crestor* and *Iressa* were announced in December 2018 and implementation is underway. This is expected to result in a level of sales decline for both brands in 2019. This evaluation is being applied retrospectively, so several existing generic products may fail and be withdrawn which could lead to a consolidation in the sector. This would leave fewer, higher-quality generics in the market thereby putting pressure on any originator brand price premiums and driving a reduction in overall medical costs.

The industry-wide growth rate is expected to be a moderate single digit percentage, following the updates of the NRDL and expanding health insurance coverage. Nevertheless, the healthcare environment in China remains dynamic. Opportunities are arising from incremental healthcare investment, strong underlying demand for AstraZeneca's more established medicines and the emergence of innovative medicines such as *Tagrisso* and *Lynparza*.

Emerging market healthcare

AstraZeneca continues to make its medicines affordable to more people on a commercially and socially sustainable basis. As, on average, almost half of medicine funding in emerging countries is paid for by the patient or their families, AstraZeneca bases its approach in these markets on an understanding of their economic circumstances and the burden placed on them by health costs. AstraZeneca is aiming to enable its Emerging Markets to deliver better and broader patient access through innovative and targeted equitable pricing strategies and practices.

AstraZeneca has a variety of access programmes around the world, each tailored to meet the needs of the local community, which include a patient's ability to pay. These include patient assistance programmes, such as *Terapia Plus* in Ukraine, *Karta Zdorovia* in Russia and *FazBem* in Brazil. Through these programmes, AstraZeneca helps qualifying patients with discounts and donations. AstraZeneca provides these

programmes in markets with limited or no public reimbursement system, no coverage beyond the most basic therapies, or where it is unlikely or only after an extended period that public reimbursement is a possible consideration.

Operations

AstraZeneca's manufacturing and supply function supports its return to growth, and its Operations 2020 plan provides a focus for its investments. These initiatives aim to ensure that AstraZeneca is able to respond to patient and market needs for its medicines. Operations 2020 was launched in 2015 to enhance supply capabilities in order to respond better to patient and market needs. It focuses on supporting the delivery of new product launches, strengthening AstraZeneca's science and technology capabilities across the globe, creating a more agile and flexible supply chain, and embedding lean principles throughout AstraZeneca's network. AstraZeneca's goal is to be recognised as a leader in the pharmaceutical supply chain by 2020.

Quality, regulation and compliance

AstraZeneca is committed to high product quality, which underpins the safety and efficacy of its medicines. AstraZeneca maintains a comprehensive quality management system to assure compliance and quality. Similarly, AstraZeneca sets strict standards for safety, health and environment at each of its sites. Manufacturing facilities and processes are subject to rigorous and continuously evolving regulatory standards. They are subject to inspections by regulatory authorities, who are authorised to mandate improvements to facilities and processes, halt production and impose conditions for production to resume.

To ensure compliance with global Good Manufacturing Practice regulations, AstraZeneca's Operations Quality team continuously reviews and strengthens the Quality Systems at its manufacturing sites through internal audit programmes, external intelligence and sharing learnings between sites. In 2018, these measures helped AstraZeneca successfully achieve zero critical observations from 48 independent inspections. AstraZeneca reviewed observations from these inspections together with the outcomes of internal audits and, where necessary, implemented improvement actions.

AstraZeneca is committed to maintaining the highest ethical standards and compliance with internal policies, laws and regulations. AstraZeneca reviews and comments upon evolving national and international compliance regulations through its membership of industry associations.

Manufacturing capabilities

AstraZeneca's principal tablet and capsule formulation sites are in the UK, Sweden, China, Puerto Rico and the US, with local/regional supply sites in Russia, Japan, Indonesia, Egypt, India, Germany, Mexico and Brazil. AstraZeneca also has major formulation sites for the global supply of parenteral and/or inhalation products in the US, Sweden, France, Australia and the UK. Most of the manufacture of APIs is delivered through the efficient use of external sourcing that is complemented by internal capability in Sweden.

For biologics, AstraZeneca's principal commercial manufacturing facilities are in the US (Frederick, Maryland; Greater Philadelphia, Pennsylvania), the UK (Speke), and the Netherlands (Nijmegen) with capabilities in process development, manufacturing and distribution of biologics, including global supply of mAbs and influenza vaccines. In Sweden, AstraZeneca's new biologics drug product manufacturing facility became available at the end of 2018.

As part of AstraZeneca's ongoing review of manufacturing capabilities and capacity, in January 2019, it made the decision to discontinue operations at the Boulder and Longmont, Colorado, manufacturing facilities to increase efficiencies in its global biologics supply chain. This step will consolidate AstraZeneca's biologic drug substance manufacturing network to one large-scale drug substance facility, the Frederick Manufacturing Center, Maryland. The closure of the sites is expected to be completed by the end of 2019 and is not expected to impact the supply or global availability of any of AstraZeneca biologic medicines. AstraZeneca will be working with the impacted employees to provide outplacement and transition support.

For small molecules AstraZeneca has constructed a new small-scale development and launch facility alongside its existing manufacturing facility in Wuxi, China. This investment supports the acceleration of delivery of AstraZeneca's new innovative medicines to patients in China and completes AstraZeneca's ability to execute across the whole life-cycle of a medicines from discovery to commercialisation.

At the end of 2018, approximately 13,000 people were employed at 29 Operations sites in 17 countries.

Intellectual property

The principal economic safeguard in the pharmaceutical industry is a well-functioning system of patent and related protection that recognises AstraZeneca's efforts and rewards innovation with appropriate protection – and allows time to generate the revenue AstraZeneca needs to reinvest in pharmaceutical innovation. Patent rights are limited by territory and duration.

A significant portion of a patent's term can be spent during R&D, before it is possible to launch the protected product. Therefore, AstraZeneca commits significant resources to establishing and defending its patent and related IP protections for inventions.

Patent process

AstraZeneca files patent protection applications for its inventions to safeguard the large investment required to obtain marketing approvals for potential new drugs. As AstraZeneca further develops a product and its uses, these new developments may necessitate new patent filings. AstraZeneca applies for patents through government patent offices around the world. These assess whether AstraZeneca's inventions meet the strict legal requirements for a patent to be granted. AstraZeneca's competitors can challenge its patents in patent offices and/or courts. AstraZeneca may face challenges early in the patent application process and throughout a patent's life. The grounds for these challenges could be the validity of a patent and/or its effective scope and are based on ever-evolving legal precedents. AstraZeneca is experiencing increased challenges in the US and elsewhere in the world (such as in Australia, Brazil, Canada, China, Europe and Japan) and there can be no guarantee of success for either party in patent proceedings.

The basic term of a patent is typically 20 years from the filing of the patent application with the relevant patent office. However, a product protected by a pharmaceutical patent may not be marketed for several years after filing, due to the duration of clinical trials and regulatory approval processes. Patent Term Extensions ("**PTEs**") are available in certain major markets, including the EU and the US, to compensate for these delays. The term of the PTE can vary from zero to five years, depending on the time taken to obtain any marketing approval. The maximum patent term, when including PTE, cannot exceed 15 years (EU) or 14 years (US) from the first marketing authorisation.

Other exclusivities

Regulatory data protection ("**RDP**" or 'data exclusivity') is an important additional form of exclusivity which is separate from, but runs in parallel to, patent exclusivity. RDP arises in respect of data which is required to be submitted to regulatory authorities to obtain marketing approvals for AstraZeneca's medicines. Significant investment is required to generate such data (for example, through conducting global clinical trials) and this proprietary data is protected from use by third parties (such as generic manufacturers) for a number of years in a limited number of countries. The period of such protection, and the extent to which it is respected, differs significantly among countries and varies depending on whether an approved drug is a small or large molecule compound. RDP is an important protection for AstraZeneca's products, and it strives to enforce its rights to it, particularly as patent rights are increasingly being challenged.

The RDP period starts from the date of the first marketing approval from the relevant regulatory authority and runs parallel to any patent protection. For small molecule drugs, RDP generally expires prior to patent expiry in all major markets.

If a product takes an unusually long time to secure marketing approval, or if patent protection has not been secured, has expired or has been lost, then RDP may be the sole right protecting a product from being copied. AstraZeneca believes that generic manufacturers should not be allowed to rely on AstraZeneca's data to support the generic product's approval or marketing until the RDP right has expired. In the EU, the RDP period is eight years followed by two years' market exclusivity.

In the US, new chemical entities are entitled to a period of five years' of RDP under the Federal Food, Drug and Cosmetic Act. This period of RDP runs parallel to any pending or granted patent protection and starts at the approval of the new application. There are circumstances where RDP could be the sole layer of exclusivity protecting a product from being copied. Further, under the Biologics License Application process, the FDA will grant 12 years' data RDP for a new biologic to an innovator manufacturer.

Under Orphan Drug laws in the EU and US, market exclusivity is granted to an innovator who gains approval for a pharmaceutical product developed to treat a rare disease. What qualifies as a rare disease differs between

the EU and US. Qualifying orphan drugs are granted 10 years' market exclusivity in the EU and seven years' market exclusivity in the US.

Compulsory licensing

Compulsory licensing (where a Patent Authority imposes a licence on the patentee) is on the increase in certain markets in which AstraZeneca operates. AstraZeneca recognises the right of developing countries to use the flexibilities in the World Trade Organization's Agreement on Trade-Related Aspects of Intellectual Property Rights (including the Doha amendment) in certain circumstances, such as a public health emergency. AstraZeneca believes this should apply only when all other ways of meeting the emergency needs have been considered and where healthcare frameworks and safeguards exist to ensure the medicines reach those who need them.

Be a great place to work

In order to achieve its goal of being a great place to work, and to further its ethical standards, in 2018 AstraZeneca: (i) encouraged improvements in scores in its employee survey (Pulse); (ii) continued development of women and increasing the representation of women in senior roles; (iii) published new global standards on inclusion and diversity, sexual harassment and bullying, reinforced by training; (iv) continued focus on workforce planning to attract critical capabilities and manage retention risks; (v) maintained listing in the Pharmaceuticals, Biotechnology and Life Sciences industry group of the Dow Jones Sustainability Index; (vi) materiality assessment reaffirmed focus and used to refine AstraZeneca's sustainability priorities; (vii) Sustainability Advisory Board met twice in 2018 to guide, recommend opportunities and provide external feedback; and (viii) continued progress towards AstraZeneca's target to source 100 per cent. renewable power by 2025.

Employees

AstraZeneca values the talents and skills of its 64,600 employees in more than 100 countries. Its people strategy supports its strategic priority of being a great place to work.

AstraZeneca is working to attract emerging talent, as well as investing in internships and recruitment opportunities globally. For example, AstraZeneca conducts a global programme to hire recent graduates for pharmaceutical technical and development, procurement, quality, engineering, IT, supply chain, and biometrics and information sciences functions. AstraZeneca also has a graduate programme in R&D, which complements its established Post Doctorate Programme for researcher recruitment. Additionally, AstraZeneca offers a 12-week internship opportunity for business school students to contribute to key initiatives in its Oncology therapeutic area.

To foster innovation, AstraZeneca seeks to harness different perspectives, talents and ideas as well as ensure that employees reflect the diversity of the communities in which AstraZeneca operates. As part of this commitment to inclusion and diversity, AstraZeneca has implemented numerous initiatives across the globe, such as unconscious bias training, the formation of various employee resource groups (such as an LGBT+ network) and updated recruitment standards to ensure diverse candidate lists.

AstraZeneca's Women as Leaders programme aims to encourage more women into senior roles – approximately 600 women had completed the programme by the end of 2018. Of those who provided feedback, 55 per cent. have either been promoted, or had their remit expanded, or been identified for future promotions. In addition, AstraZeneca has developed women's networks in most countries, continued to hold women's summits in various locations around the world and continued to support mentoring relationships, for example introducing mentoring by senior women for emerging talent in Operations.

Code of Ethics and Policy Framework

AstraZeneca is committed to employing high ethical standards when carrying out all aspects of its business globally. AstraZeneca's Code of Ethics (the "**Code**") is based on AstraZeneca's company Values, expected behaviours and key policy principles. It empowers employees to make decisions in the best interests of the Group and the people AstraZeneca serves, now and in the long term, by outlining AstraZeneca's commitments in simple terms and focusing on why these commitments matter. The Code also guides employees on how to make the best day-to-day choices and how to act in a consistent, responsible way, worldwide. There are two mandatory training courses dedicated to the Code: one is for new starters; the second is the annual training for

all employees, reminding them of the key commitments. In 2018, 100 per cent. of all active employees completed the annual training on the Code.

The Code includes four high-level Global Policies covering Science, Interactions, Workplace and Sustainability. These Global Policies will continue to be complemented by underlying Global Standards and will, over time, replace the current suite of Global Policies. AstraZeneca's policy framework also includes additional requirements at the global, local and business unit level to support employees in their daily work.

Ethical sales and marketing

AstraZeneca is committed to employing high ethical standards of sales and marketing practice worldwide, in line with its policy framework. AstraZeneca maintains a robust compliance programme in its efforts to ensure compliance with all applicable laws, regulations and adopted industry codes. AstraZeneca's compliance programme is delivered by dedicated compliance professionals who advise on and monitor adherence to its policy framework. These professionals also support AstraZeneca's line managers locally in ensuring that their staff meet its standards. A network of nominated signatories reviews AstraZeneca's promotional materials and activities against applicable requirements. AstraZeneca's Internal Audit Services, in partnership with external audit experts, also conduct compliance audits on selected marketing companies. AstraZeneca's reporting in relation to ethical sales and marketing is assured by Bureau Veritas UK Limited ("**Bureau Veritas**"), an independent professional services company that specialises in quality, environmental, health, safety and social accountability. Bureau Veritas operates a certified Quality Management System which complies with the requirements of ISA 9001:2008.

Approximately 36,100 employees are engaged in AstraZeneca's commercial activities and, in 2018, AstraZeneca identified four confirmed breaches of external sales and marketing regulations or codes (2017: six). There were 2,042 instances, most of them minor, of non-compliance with the Code or supporting requirements in AstraZeneca's Commercial Regions, including instances by employees and third parties (2017: 1,431). AstraZeneca removed a total of 169 employees and third parties from their roles as a result of these breaches (a single breach may involve more than one person). AstraZeneca also formally warned 534 others and provided further guidance or coaching on its policies to 1,865 more. The Audit Committee are provided with the breach statistics on a quarterly basis. Further commentary on the most serious breaches is also provided to the Audit Committee.

Anti-bribery/anti-corruption

Anti-bribery/anti-corruption is a key element of AstraZeneca's policy framework, with principles and requirements underpinning the Code commitment that it does not tolerate bribery or any other form of corruption. AstraZeneca conveyed its commitment to ethical behaviour in the 2018 annual Code training, reinforced through anti-bribery/anti-corruption training materials delivered and made available to relevant employees and third parties.

Bribery and corruption remains a business risk as AstraZeneca launches new medicines in markets across the globe and enters into partnerships and collaborations. When working with third parties, AstraZeneca is committed to working with only those who embrace high standards of ethical behaviour consistent with its own. Bribery and corruption risk is a focus of AstraZeneca's third-party risk management process, as well as its Business Development due diligence procedures. It is also a focus of its monitoring and audit programmes. Global Compliance monitors a range of commercial activities associated with bribery and corruption risk, and the majority of marketing company audits include anti-bribery/anti-corruption work programmes.

Transparency reporting

AstraZeneca is committed to the highest standards of conduct in all its operations, including the disclosure of payments to healthcare practitioners, healthcare organisations and patient groups, with full transparency where recipients have provided consent and in accordance with all current obligations covering the 43 markets with reporting requirements. In the US, Europe, Australia and Japan AstraZeneca's external transparency reporting meets the requirements of the Physician Payments Sunshine Act, European Federation of Pharmaceutical Industries and Associations Disclosure Code, Medicines Australia Code of Practice, and the Japanese Pharmaceutical Manufacturers Association Disclosure Code, as well as applicable local and state transparency requirements.

Bioethics and responsible research

AstraZeneca's commitment to working in a transparent and ethical manner is essential to achieving scientific leadership and delivering life-changing medicines. 'Bioethics' refers to the range of ethical issues that arise from the study and practice of biological and medical science, and AstraZeneca's Bioethics Policy sets out its principles in key subject matter areas. These principles apply to all of AstraZeneca's research activity, whether conducted by it or by third parties acting on its behalf.

AstraZeneca's Bioethics Advisory Group ("**BAG**") is sponsored by the Chief Medical Officer, and exists to oversee the operation of the Bioethics Policy. It acts as a source of bioethical advice to the business, bringing together the subject matter leads for each of the key bioethical areas, supported by other experts and specialists. BAG receives reports on governance and practice from subject matter leads, responds to requests for advice and support from the business, and carries out horizon-scanning activities to identify emerging scientific, technological and regulatory issues. BAG met six times in 2018. Ethical discussions in 2018 included the potential therapeutic use of human stem cells in patients, the implications of continuing advances in precise genome technologies, and issues around consent and withdrawal of consent for use of patient samples and data.

Patient safety

One of AstraZeneca's core values is to put patients first and, by detecting, assessing, understanding and preventing adverse effects or any other drug-related problems not identified during the development process, its pharmacovigilance processes and systems seek to minimise the risks and maximise the benefits of its medicines for patients.

Research use of human biological samples

The use of human biological samples, such as solid tissue, biofluids and their derivatives, plays a vital role in developing a deeper understanding of human diseases and their underlying mechanisms, which helps AstraZeneca develop effective, new and personalised medicines.

When AstraZeneca conducts this important research, it maintains policies and processes to ensure that it complies with the law, meets regulatory concerns and maintains ethical standards. AstraZeneca places an emphasis on informed consent that protects the rights and expectations of donors and families throughout the process of its acquisition, use, storage and disposal of the samples. Protecting the confidentiality of a donor's identity is of the utmost importance, and a key part of AstraZeneca's process includes the coding of biological samples and associated data (including genetic data).

In rare circumstances, AstraZeneca may use human foetal tissue ("**hFT**") or human embryonic stem cells ("**hESC**"). In these circumstances, an internal review of the scientific validity of the research proposal will be conducted and permission to use the tissue will be granted only when no other scientifically reasonable alternative is available. AstraZeneca also insists that its third party vendors adopt the highest ethical standards and it rigorously assess the ability of tissue suppliers to meet its quality and ethical expectations. AstraZeneca is committed to minimising the use of foetal tissue by exploring technological alternatives.

In 2018, an additional research proposal that includes use of cells derived from hFT was approved, resulting in three projects using hFT having progressed as at 31 December. An additional three projects using hESC were approved in 2018, resulting in nine projects using 13 different hESC lines or derived cells having been approved to date.

Animal research

AstraZeneca is committed to helping the public understand the continuing need for animals in research, and its approach to replacing, reducing and refining its use of animals.

Ethical supply chain management

Every employee and contractor who sources goods and services on behalf of AstraZeneca is expected to follow responsible business processes, which are embedded into its newly updated Global Standard for the Procurement of Goods and Services. All of AstraZeneca's procurement professionals receive detailed training on responsible procurement.

AstraZeneca's ethical standards are integral to its procurement and partnering activities and it monitors compliance through assessments and improvement programmes. AstraZeneca works only with those suppliers whose standards of ethical behaviour are consistent with its own. AstraZeneca will not use suppliers who are unable to meet its standards.

To achieve this, AstraZeneca has an established process for third party risk management. This process assesses risk based upon defined criteria. These include risks related to bribery and corruption, data privacy, the environment and wages. Each step of the process provides an additional level of assessment, and AstraZeneca conducts more detailed assessments on those relationships identified as higher risk. Through this risk-mitigation process, AstraZeneca seeks to better understand the partner's risk approach and seek to ensure the partner understands and can meet AstraZeneca's standards. AstraZeneca conducted a total of 12,967 assessments in 2018, taking its total number of assessments to 27,257 since it established this process in May 2014. Of the assessments undertaken in 2018, 3,390 were in the Asia Pacific region, 4,035 in Europe and 3,965 in the Americas. The remaining 1,577 assessments relate to global suppliers and those based in the Middle East and Africa.

In 2018, AstraZeneca conducted 45 audits on high-risk suppliers (external manufacturing partners), seeking to ensure that they employ appropriate practices and controls. 86 per cent. of these suppliers met AstraZeneca's expectations, with a further 14 per cent. implementing improvement plans to address minor instances of non-compliance. Through AstraZeneca's due diligence process, it rejected seven suppliers because of reputational concerns due to high anti-bribery/anti-corruption risk.

Safety, health and wellbeing

AstraZeneca works to promote a safe, healthy and energising work environment for employees and partners. AstraZeneca's standards apply globally and are stated in its Code. Due diligence includes establishing and monitoring a set of safety, health and wellbeing targets aimed at supporting AstraZeneca's people and keeping it among the sector leaders in performance. AstraZeneca's reporting in this area is assured by Bureau Veritas.

AstraZeneca made good progress against its strategic targets in 2018, achieving a 26 per cent. reduction in the work-related injury rate and a 9 per cent. reduction in vehicle collision rate from the 2015 baseline. In addition, there were no work-related fatalities during 2018. Building on its previous success in establishing a culture of health and wellbeing, AstraZeneca is continuing to focus on active health promotion. AstraZeneca has programmes to address all four essential health activities – healthy eating and drinking, physical activity, tobacco cessation and mental wellbeing – at 65 per cent. of its sites. In 2018, AstraZeneca carried out several activities and initiatives focused on continuous improvements in key risk areas, including driver safety (AstraZeneca's highest risk for significant injury and fatalities), behavioural safety, ergonomics, office safety, fall prevention, workplace pressure management and work-life balance.

Community investment

Wherever AstraZeneca works in the world, it aims to make a positive impact on its communities. AstraZeneca's Global Standard on Contributions encompasses community investment and provides guidance to ensure a consistent, transparent and ethical approach around the world, based on local need. AstraZeneca's activities are focused on healthcare in the community and supporting science education. They include financial and non-financial contributions. In 2018, AstraZeneca gave more than US\$57 million (2017: US\$25 million) through its community investment activities to more than 1,000 non-profit organisations in 70 countries. The increase reflects a change in practice with more large multi-year agreements with payments being made in the first year if the agreement. The amount includes more than US\$17.5 million (2017: \$4 million) for product donations that were given in support of public health needs and disaster relief. The increase reflects changes in the volume and mix of product donated. In addition to these community investments, AstraZeneca also donated more than US\$686 million (2017: US\$401 million) of medicines in connection with patient assistance programmes around the world, the largest of which is its AZ&Me programme in the US.

AstraZeneca's global disaster relief partner is the British Red Cross. In 2018, AstraZeneca entered into a two-year partnership that will support humanitarian aid to people affected by armed conflict in Northern Nigeria. AstraZeneca's global product donation partners are Americares, Direct Relief International and Health Partners International of Canada.

In 2018, AstraZeneca launched the Step Up! Young Health Global Grants Programme. Designed to complement its work in the field of adolescent health and NCD prevention, this programme offered grants of

up to US\$10,000 to non-profit organisations that are innovating to improve the health and wellbeing of young people. A total of US\$160,375 of funding was committed through this programme in 2018 for 17 projects in 14 countries.

AstraZeneca continues to support Connections for Cardiovascular HealthSM, a programme of the AstraZeneca HealthCare Foundation that was launched in 2010 to address heart health in the US. In 2018, the AstraZeneca HealthCare Foundation provided US\$1.16 million in grants to 11 non-profit organisations for programmes that aim to help prevent, better manage and reduce cardiovascular disease.

Making a positive impact on AstraZeneca's communities is also about volunteering. AstraZeneca encourages its employees to volunteer and support their efforts with one day's leave for community service. In 2018, AstraZeneca's employees volunteered more than 39,000 hours on community projects in countries around the world.

Young Health Programme

NCDs prevention among young people continued to be an area of focus as AstraZeneca marked the ninth year of its award-winning Young Health Programme ("YHP"). Despite the fact that more than two thirds of premature deaths from NCDs can be linked to behaviours that first began in adolescence, young people and their health continues to be an under-recognised, under-served and under-researched component of the global health agenda. In 2018, AstraZeneca reached nearly 335,000 young people with health information on NCDs and risk behaviours and trained more than 5,500 peer educators and healthcare workers. In partnership with local governmental and non-governmental groups, AstraZeneca launched new programmes in Indonesia, Serbia, Turkey and Australia and approved the development of new programmes in Vietnam, Myanmar, Mexico and Panama. This brings the total number of AstraZeneca's developing and active YHP initiatives to 20.

AstraZeneca supported its partners, NCD Child and Plan International, as they advocated for the inclusion of adolescent health and NCD prevention in the Political Declaration on NCDs and at the United Nation's Third High Level Meeting on NCDs. AstraZeneca invested in new research on adolescent risk behaviours, policy recommendations and health economic analyses to support the argument for additional investment in and attention to NCD prevention among young people. It also continued to mentor and support the development of young global health leaders by sending a delegation of 20 young people to the One Young World Summit in The Hague, Netherlands.

YHP was named Community Investment Program of the Year by Ethical Corporation's 2018 Responsible Business Awards.

Legal and Arbitration Proceedings

Save as disclosed in Note 29 to AstraZeneca's consolidated financial statements for the year ended 31 December 2018 on pages 194 to 199 (inclusive) of AstraZeneca's Annual Report and Form 20-F Information 2018 and in Note 5 to AstraZeneca's 2019 Q1 Results dated 26 April 2019, which have been incorporated by reference into this Base Prospectus there are no governmental, legal or arbitration proceedings, (including any such proceedings which are pending or threatened, of which AstraZeneca is aware), which may have, or have had during the 12 months prior to the date of this Base Prospectus, a significant effect on the financial position or profitability of AstraZeneca and its Subsidiaries.

Group Structure

AstraZeneca is the ultimate holding company of the Group. The principal subsidiaries of AstraZeneca, being those subsidiaries which account for more than (i) 10 per cent. of the Group's operating income; or (ii) 10 per cent. of the Group's assets; or (iii) if the Group's total investment in the subsidiary exceeds 10 per cent. of the Group's assets as at 31 December 2018, are listed below.

<u>At 31 December 2018</u>	<u>Country</u>	<u>Percentage of Voting Share Capital Held (per cent.)</u>
United Kingdom		
AstraZeneca Intermediate Holdings Limited.....	England	100
AstraZeneca UK Limited	England	100
AstraZeneca Treasury Limited	England	100

KuDOS Pharmaceuticals Limited	England	100
Continental Europe		
AstraZeneca AB	Sweden	100
AstraZeneca Biotech AB	Sweden	100
Acerta Pharma B.V.	The Netherlands	55
The Americas		
IPR Pharmaceuticals Inc.	Puerto Rico	100
ZS Pharma Inc.	United States	100
AstraZeneca Pharmaceuticals LP	United States	100
MedImmune, LLC.....	United States	100

Major Shareholdings

As at 11 June 2019, the following had disclosed an interest in the issued ordinary share capital of AstraZeneca in accordance with the requirements of section 5.1.2 or 5.1.5 of the United Kingdom Listing Authority's Disclosure Rules and Transparency Rules:

Shareholder	Number of shares	Date of disclosure to AstraZeneca	Percentage of issued share capital (%)
BlackRock, Inc.	100,885,181	4 Dec 2009	7.69
The Capital Group Companies, Inc.	63,802,495	17 July 2018	4.864
Investor AB	51,587,810	4 April 2019	3.93

Board of Directors

The Directors and Secretary of AstraZeneca as at 11 June 2019, their functions in AstraZeneca and their principal outside activities (if any) of significance to AstraZeneca are as follows:

Name	Function within AstraZeneca	Principal Outside Activity (if any) of Significance to AstraZeneca
Pascal Soriot.....	Executive Director and Chief Executive Officer	None
Marc Dunoyer	Executive Director and Chief Financial Officer	Director of Orchard Therapeutics
Leif Johansson.....	Non-Executive Chairman, Chairman of the Nomination and Governance Committee and Member of the Remuneration Committee	Member of the European Round Table of Industrialists. Board member of Ecolan AB and Autoliv, Inc. Member of the Royal Swedish Academy of Engineering Sciences. Member of the Council of Advisors, Boao Forum for Asia
Graham Chipchase	Senior Independent Non-Executive Director, Chairman of the Remuneration Committee and Member of the Nomination and Governance Committee	Chief Executive Officer of Brambles Limited
Geneviève Berger.....	Non-Executive Director and Member of the Science Committee	Director of L'Air Liquide S.A. Chief Research Officer at Firmenich, SA, Geneva, Switzerland
Philip Broadley	Non-Executive Director, Chairman of the Audit Committee, Member of the Remuneration Committee and Member of the Nomination and Governance Committee	Chair of the Audit Committee of Legal & General Group plc. Treasurer of the London Library. Chairman of the Board of Governors of Eastbourne College
Deborah DiSanzo.....	Non-Executive Director and Member of the Audit Committee	Harvard University Advanced Leadership Fellow
Sheri McCoy.....	Non-Executive Director and Member of the Audit Committee and the Remuneration Committee	Member of the board of Stryker Corporation, Kimberly-Clark and NovoCure. Industrial Advisor for EQT Partners where she chairs Certara. Trustee for Stonehill College, Easton, Massachusetts
Tony Mok.....	Non-Executive Director and Member of the Science Committee	Non-Executive Director of Hutchinson China MediTech Limited and a co-founder and Chairman of Sanomics Limited
Nazneen Rahman	Non-Executive Director, Chairman of the Science Committee and Member of the Nomination and the Governance Committee	None
Marcus Wallenberg.....	Non-Executive Director and Member of the Science Committee	Chairman of Skandinaviska Enskilda Banken AB, Saab AB, and Foundation Asset Management AB. Member of the boards of Investor AB, Temasek Holdings Limited, and the Knut and Alice Wallenberg Foundation
Adrian Kemp.....	Company Secretary	None

The business address of each of the Directors and the Company Secretary referred to above is 1 Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge CB2 0AA.

There are no potential conflicts of interest between the duties to the Issuer of its Directors and the Company Secretary and their private interests and other duties.

Recent Developments

The following paragraphs update the information in the Annual Report and Form 20-F Information 2018, which has been incorporated by reference.

First quarter results

On 26 April 2019, AstraZeneca announced its first quarter results, which included the following:

- Product sales growth of 10 per cent. (14 per cent. at CER) to US\$5,465 million
- Total revenue for the first quarter was US\$5,491 million, up 11 per cent. at CER compared to the first quarter of 2018
- Reported earnings per share ("**EPS**") was US\$0.47, up 90 per cent. at CER compared to the first quarter of 2018
- Core EPS was US\$0.89, up 100 per cent. at CER compared to the first quarter of 2018

Upon announcing its first quarter results, AstraZeneca announced its 2019 strategic priorities. For further information, see "*Strategy*" above.

Pipeline developments

On 1 February 2019, AstraZeneca announced that the Committee for Medicinal Products for Human Use ("**CHMP**") of the European Medicines Agency had recommended a new indication for the marketing authorisation of *Forxiga* (dapagliflozin), after adopting a positive opinion for use as an oral adjunct treatment to insulin in adults with type-1 diabetes.

On 5 February 2019, AstraZeneca and its global biologics research and development arm, MedImmune, announced that the European Medicines Agency had granted access to its PRIME (PRiority MEDicines) scheme for MEDI8897, an extended half-life respiratory syncytial virus ("**RSV**") F monoclonal antibody being developed for the prevention of lower respiratory tract infection ("**LRTI**") caused by RSV.

On 5 February 2019, AstraZeneca and its global biologics research and development arm, MedImmune, also announced that the US Food and Drug Administration (the "**FDA**") had granted Breakthrough Therapy Designation for MEDI8897, an extended half-life RSV F monoclonal antibody being developed for the prevention of LRTI caused by RSV.

On 6 February 2019, AstraZeneca announced that the FDA had granted Orphan Drug Designation to *Fasenra* (benralizumab) for the treatment of hypereosinophilic syndrome ("**HES**"). HES is a group of rare, potentially fatal disorders characterised by high numbers of eosinophils in blood and tissues, which can cause progressive damage to any organ in the body.

On 25 February 2019, AstraZeneca announced that the Phase III THEMIS trial met its primary endpoint and demonstrated that *Brilinta* (ticagrelor), taken in conjunction with aspirin, showed a statistically-significant reduction in a composite of major adverse cardiovascular events compared to aspirin alone.

On 26 February 2019, AstraZeneca and MSD Inc., Kenilworth, N.J., US (known as Merck & Co., Inc. inside the US and Canada) announced positive results from the Phase III POLO trial that showed a statistically-significant and clinically-meaningful improvement in progression-free survival with *Lynparza* (olaparib) versus a placebo. The safety and tolerability profile of *Lynparza* was consistent with previous trials.

On 1 March 2019, AstraZeneca and MSD, Inc. announced that the CHMP of the European Medicines Agency had adopted a positive opinion, recommending the use of *Lynparza* (olaparib) tablets as monotherapy for the treatment of adult patients with germline BRCA1/2-mutations, who have human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer.

On 18 March 2019, AstraZeneca announced that the FDA had granted Orphan Drug Designation for saracatinib, a potential new medicine for the treatment of idiopathic pulmonary fibrosis, a type of lung disease that results in scarring (fibrosis) of the lungs. *Saracatinib* is an inhibitor of src kinase which regulates broad cell functions including cell growth and cell differentiation. *Saracatinib* has completed Phase I development.

On 25 March 2019, AstraZeneca announced that the European Commission had approved *Forxiga* (dapagliflozin) for use in type-1 diabetes as an adjunct to insulin in patients with a BMI of more than or equal to 27 kg/m², when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy.

On 27 March 2019, AstraZeneca announced that the Japanese Ministry of Health, Labour and Welfare had approved *Forxiga* (dapagliflozin) as an oral adjunct treatment to insulin for adults with type-1 diabetes.

On 1 April 2019, AstraZeneca and MSD, Inc. announced that the FDA had granted Breakthrough Therapy Designation for the MEK 1/2 inhibitor and potential new medicine *selumetinib*.

On 10 April 2019, AstraZeneca and MSD Inc. announced that the European Commission had approved *Lynparza* (olaparib) as a monotherapy for the treatment of adult patients with germline BRCA1/2-mutations (gBRCAm), and who have human epidermal growth factor receptor 2 (HER2)-negative locally-advanced or metastatic breast cancer.

On 29 April 2019, AstraZeneca and MSD Inc. announced that the CHMP of the European Medicines Agency had adopted a positive opinion, recommending *Lynparza* (olaparib) as a 1st line maintenance treatment of BRCA-mutated advanced ovarian cancer.

On 3 May 2019, AstraZeneca announced that the FDA had approved *Qternmet XR* (dapagliflozin, saxagliptin and metformin hydrochloride) extended release tablets as an oral adjunct treatment to diet and exercise to improve glycaemic control in adults with type-2 diabetes.

On 8 May 2019, AstraZeneca and Daiichi Sankyo Company, Limited ("**Daiichi Sankyo**") announced positive top-line results for the pivotal Phase II DESTINY-Breast01 trial of *trastuzumab deruxtecan* (DS-8201). The HER2-targeting antibody drug conjugate and potential new medicine was evaluated in patients with HER2-positive, unresectable and/or metastatic breast cancer previously treated with trastuzumab emtansine.

On 10 May 2019, AstraZeneca announced top-line results from the pooled cardiovascular safety analyses of the global Phase III programme for roxadustat, a first-in-class hypoxia-inducible-factor prolyl hydroxylase inhibitor. The global pivotal Phase III trials evaluated roxadustat for treatment of anaemia in patients with chronic kidney disease across the non-dialysis-dependent, incident (newly-initiated) dialysis, and stable dialysis patient groups.

On 3 June 2019, AstraZeneca and MSD Inc. announced detailed results from the Phase III POLO trial at the 2019 American Society of Clinical Oncology Annual Meeting in Chicago, US. The POLO trial tested *Lynparza* (olaparib) tablets as 1st-line maintenance monotherapy for patients with germline BRCA-mutated (gBRCAm) metastatic adenocarcinoma of the pancreas (pancreatic cancer) whose disease had not progressed following standard-of-care platinum-based first-line chemotherapy. Results from the trial showed a statistically-significant and clinically-meaningful improvement in progression-free survival for *Lynparza* versus placebo, improving the time without disease progression by a median of 7.4 months for patients treated with *Lynparza* versus 3.8 months for those on placebo (HR 0.53 {95per cent. CI, 0.35-0.82}, p=0.004). More than twice as many patients showed no disease progression both at one year (34 per cent. on *Lynparza* versus 15 per cent. on placebo) and two years (22 per cent. versus 10 per cent., respectively).

On 6 June 2019, AstraZeneca announced positive results from the Phase III ELEVATE-TN trial of *Calquence* (acalabrutinib) in patients with previously-untreated chronic lymphocytic leukaemia ("**CLL**"), the most common type of leukaemia in adults. This is the second *Calquence* pivotal trial in CLL to meet its primary endpoint early, following the positive results of the ASCEND trial, announced in May.

Commercial developments

On 25 January 2019, AstraZeneca and its global biologics research and development arm, MedImmune, completed an agreement with Swedish Orphan Biovitrum AB (publ) ("**Sobi**") for the sale of its US rights to *Synagis* (palivizumab), used for the prevention of serious LRTI caused by RSV. Sobi will commercialise *Synagis* in the US and around 130 AstraZeneca employees have transferred to Sobi as part of the transaction.

Sobi will also have the right to participate in payments from the US profits or losses for potential new medicine MEDI8897 in development for RSV-induced LRTI. AstraZeneca will continue to develop MEDI8897 in collaboration with Sanofi Pasteur, the vaccines division of Sanofi S.A.

On 29 March 2019, AstraZeneca announced that it had entered into a global development and commercialisation collaboration agreement with Daiichi Sankyo for trastuzumab deruxtecan (DS-8201), a proprietary antibody-drug conjugate and potential new targeted medicine for cancer treatment. AstraZeneca and Daiichi Sankyo will jointly develop and commercialise trastuzumab deruxtecan worldwide, except in Japan where Daiichi Sankyo will maintain exclusive rights. Daiichi Sankyo will be solely responsible for manufacturing and supply.

As part of the agreement, AstraZeneca will pay Daiichi Sankyo an upfront payment of US\$1.35bn, contingent payments of up to US\$5.55bn which include US\$3.8bn for potential successful achievement of future regulatory and other milestones, as well as US\$1.75bn for sales-related milestones.

As announced on 29 March 2019, AstraZeneca funded part of the purchase price in relation to the agreement through a placing of new ordinary shares in AstraZeneca with both existing and new institutional investors.

TAXATION

United Kingdom Taxation

The following is a summary of the United Kingdom withholding taxation treatment at the date hereof in relation to payments of principal and interest in respect of the Notes. It is based on current law and the practice of Her Majesty's Revenue and Customs ("HMRC"), which may be subject to change, sometimes with retrospective effect. The comments do not deal with other United Kingdom tax aspects of acquiring, holding or disposing of Notes. The comments relate only to the position of persons who are absolute beneficial owners of the Notes. Prospective Noteholders should be aware that the particular terms of issue of any series of Notes as specified in the relevant Final Terms may affect the tax treatment of that and other series of Notes. The following is a general guide for information purposes and should be treated with appropriate caution. It is not intended as tax advice and it does not purport to describe all of the tax considerations that may be relevant to a prospective purchaser. Noteholders who are in any doubt as to their tax position should consult their professional advisers. Noteholders who may be liable to taxation in jurisdictions other than the United Kingdom in respect of their acquisition, holding or disposal of the Notes are particularly advised to consult their professional advisers as to whether they are so liable (and if so under the laws of which jurisdictions), since the following comments relate only to certain United Kingdom taxation aspects of payments in respect of the Notes. In particular, Noteholders should be aware that they may be liable to taxation under the laws of other jurisdictions in relation to payments in respect of the Notes even if such payments may be made without withholding or deduction for or on account of taxation under the laws of the United Kingdom.

Withholding Tax on UK Source Interest

UK Notes listed on a recognised stock exchange

The Notes issued by the Issuer which carry a right to interest ("UK Notes") will constitute "quoted Eurobonds" provided they are and continue to be listed on a recognised stock exchange (within the meaning of section 1005 of the Income Tax Act 2007 (the "Act")) or admitted to trading on a "multilateral trading facility" (within the meaning of section 987 of the Act). Whilst the UK Notes are and continue to be quoted Eurobonds, payments of interest on the UK Notes may be made without withholding or deduction for or on account of United Kingdom income tax.

The London Stock Exchange is a recognised stock exchange, and accordingly the Notes will constitute quoted Eurobonds provided they are and continue to be included in the United Kingdom official list and admitted to trading on the Regulated Market of that Exchange.

In all cases falling outside the exemption described above, interest on the UK Notes may fall to be paid under deduction of United Kingdom income tax at the basic rate (currently 20 per cent.) subject to such relief or exemption as may be available. However, this withholding will not apply if the relevant interest is paid on Notes with a maturity date of less than one year from the date of issue and which are not issued under arrangements the effect of which is to render such Notes part of a borrowing with a total term of a year or more.

Other Rules relating to Withholding in respect of United Kingdom Tax

1. Notes may be issued at an issue price of less than 100 per cent of their principal amount. Any discount element on any such Notes will not generally be subject to any United Kingdom withholding tax pursuant to the provisions mentioned above.
2. Where Notes are to be, or may fall to be, redeemed at a premium, as opposed to being issued at a discount, then any such element of premium may constitute a payment of interest. Payments of interest are subject to United Kingdom withholding tax as outlined above.
3. Where interest has been paid under deduction of United Kingdom income tax, Noteholders who are not resident in the United Kingdom may be able to recover all or part of the tax deducted if there is an appropriate provision in any applicable double taxation treaty.
4. The references to "interest" in this *United Kingdom Taxation* section mean "interest" as understood in United Kingdom tax law. The statements in this *United Kingdom Taxation* section do not take any account of any different definitions of "interest" or "principal" which may prevail under any other law or which may be created by the terms and conditions of the Notes or any related documentation. Noteholders should seek their own professional advice as regards the withholding tax treatment of any

payment on the Notes which does not constitute "interest" or "principal" as those terms are understood in United Kingdom tax law. Where a payment on a Note does not constitute (or is not treated as) interest for United Kingdom tax purposes, and the payment has a United Kingdom source, it would potentially be subject to United Kingdom withholding tax if, for example, it constitutes (or is treated as) an annual payment or a manufactured payment for United Kingdom tax purposes (which will be determined by, amongst other things, the terms and conditions specified by the Final Terms of the Note). In such a case, the payment may fall to be made under deduction of United Kingdom tax (the rate of withholding depending on the nature of the payment), subject to such relief as may be available following a direction from HMRC pursuant to the provisions of any applicable double taxation treaty, or to any other exemption which may apply.

5. The above description of the United Kingdom withholding tax position assumes that there will be no substitution of the Issuer (pursuant to Condition 16(c) of the Notes or otherwise) and does not consider the tax consequences of any such substitution.

The Proposed Financial Transactions Tax ("FTT")

On 14 February 2013, the European Commission published a proposal (the "Commission's Proposal") for a directive for a common financial transactions tax (the "FTT") in Belgium, Germany, Estonia, Greece, Spain, France, Italy, Austria, Portugal, Slovenia and Slovakia (the "participating Member States"). However, Estonia has since stated that it will not participate.

The Commission's Proposal has very broad scope and could, if introduced, apply to certain dealings in the Notes (including secondary market transactions) in certain circumstances. The issuance and subscription of Notes should, however, be exempt.

Under the Commission's Proposal the FTT could apply in certain circumstances to persons both within and outside of the participating Member States. Generally, it would apply to certain dealings in the Notes where at least one party is a financial institution, and at least one party is established in a participating Member State. A financial institution may be, or be deemed to be, "established" in a participating Member State in a broad range of circumstances, including (a) by transacting with a person established in a participating Member State or (b) where the financial instrument which is subject to the dealings is issued in a participating Member State.

The FTT proposal remains subject to negotiation between participating Member States. It may therefore be altered prior to any implementation, the timing of which remains unclear. Additional EU Member States may decide to participate.

Prospective holders of Notes are advised to seek their own professional advice in relation to the FTT.

SUBSCRIPTION AND SALE

Notes may be sold from time to time by the Issuer to any one or more of Barclays Bank PLC, Citigroup Global Markets Limited, Deutsche Bank AG, London Branch, Goldman Sachs International, HSBC Bank plc, J.P. Morgan Securities plc, Merrill Lynch International, Mizuho International plc and Morgan Stanley & Co. International plc (the "**Dealers**"). The arrangements under which Notes may from time to time be agreed to be sold by the Issuer to, and purchased by, Dealers are set out in an amended and restated dealer agreement dated 12 June 2019 (the "**Dealer Agreement**") and made between the Issuer and the Dealers. Any such agreement will, *inter alia*, make provision for the form and terms and conditions of the relevant Notes, the price at which such Notes will be purchased by the Dealers and the commissions or other agreed deductibles (if any) payable or allowable by the Issuer in respect of such purchase. The Dealer Agreement makes provision for the resignation or termination of appointment of existing Dealers and for the appointment of additional or other Dealers either generally in respect of the Programme or in relation to a particular Tranche of Notes.

United States of America

The Notes have not been, and will not be, registered under the Securities Act or with any securities regulatory authority of any state or other jurisdiction of the United States and may not be offered, delivered or sold within the United States or to, or for the account or benefit of, U.S. persons (as defined in Regulation S) except in certain transactions exempt from the registration requirements of the Securities Act.

The Notes are subject to U.S. tax law requirements and may not be offered, sold or delivered within the United States or its possessions or to a United States person, except in certain transactions permitted by U.S. tax regulations. Terms used in this paragraph have the meanings given to them by the United States Internal Revenue Code and regulations thereunder.

Each Dealer has agreed that, except as permitted by the Dealer Agreement, it will not offer, sell or deliver Notes, (i) as part of their distribution at any time or (ii) otherwise until 40 days after the completion of the distribution of the Notes comprising the relevant Tranche, as certified to the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent or the Issuer by such Dealer (or, in the case of a sale of a Tranche of Notes to or through more than one Dealer, by each of such Dealers as to the Notes of such Tranche purchased by or through it, in which case the Principal Paying Agent or, as the case may be, the CMU Lodging and Paying Agent or the Issuer shall notify each such Dealer when all such Dealers have so certified) within the United States or to, or for the account or benefit of, U.S. persons, and such Dealer will have sent to each dealer to which it sells Notes during the distribution compliance period relating thereto a confirmation or other notice setting forth the restrictions on offers and sales of the Notes within the United States or to, or for the account or benefit of, U.S. persons.

In addition, until 40 days after the commencement of the offering of Notes comprising any Tranche, any offer or sale of Notes within the United States by any dealer (whether or not participating in the offering) may violate the registration requirements of the Securities Act.

Prohibition of Sales to EEA Retail Investors

Unless the applicable Final Terms in respect of any Notes specifies the "Prohibition of Sales to EEA Retail Investors" as "Not Applicable", each Dealer has represented and agreed, and each further Dealer appointed under the Programme will be required to represent and agree, that it has not offered, sold or otherwise made available and will not offer, sell or otherwise make available any Notes which are the subject of the offering contemplated by this Base Prospectus as completed by the applicable Final Terms in relation thereto to any retail investor in the European Economic Area. For the purposes of this provision the expression "**retail investor**" means a person who is one (or more) of the following:

- a) a retail client as defined in point (11) of Article 4(1) of MiFID II; or
- b) a customer within the meaning of Directive 2002/92/EC, as amended or superseded, where that customer would not qualify as a professional client as defined in point (10) of Article 4(1) of MiFID II; and
- c) not a qualified investor as defined in the Prospectus Directive.

If the Final Terms in respect of any Notes specifies "Prohibition of Sales to EEA Retail Investors" as "Not Applicable", in relation to each Member State of the European Economic Area which has implemented the

Prospectus Directive (each, a "**Relevant Member State**"), each Dealer has represented and agreed, and each further Dealer appointed under the Programme will be required to represent and agree, that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the "**Relevant Implementation Date**") it has not made and will not make an offer of Notes which are the subject of the offering contemplated by this Base Prospectus as completed by the Final Terms in relation thereto to the public in that Relevant Member State except that it may, with effect from and including the Relevant Implementation Date, make an offer of such Notes to the public in that Relevant Member State:

- a) *Qualified investors*: at any time to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- b) *Fewer than 150 offerees*: at any time to fewer than 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the relevant Dealer or Dealers nominated by the Issuer for any such offer; or
- c) *Other exempt offers*: at any time in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of Notes referred to in (a) to (c) above shall require the Issuer or any Dealer to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive. For the purposes of this provision, the expression an "**offer of Notes to the public**" in relation to any Notes in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the Notes to be offered so as to enable an investor to decide to purchase or subscribe the Notes, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression Prospectus Directive includes any relevant implementing measure in the Relevant Member State.

Selling Restrictions Addressing Additional United Kingdom Securities Laws

Each Dealer has represented, warranted and undertaken and each further Dealer appointed under the Programme will be required to represent, warrant and undertake, that:

- (a) ***No deposit-taking in relation to any Notes having a maturity of less than one year:***
 - (i) it is a person whose ordinary activities involve it in acquiring, holding, managing or disposing of investments (as principal or agent) for the purposes of its business; and
 - (ii) it has not offered or sold and will not offer or sell any Notes other than to persons:
 - (A) whose ordinary activities involve them in acquiring, holding, managing or disposing of investments (as principal or agent) for the purposes of their businesses; or
 - (B) who it is reasonable to expect will acquire, hold, manage or dispose of investments (as principal or agent) for the purposes of their businesses,

where the issue of the Notes would otherwise constitute a contravention of Section 19 of the FSMA by the Issuer;

- (b) ***Financial promotion:***

it has only communicated or caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) received by it in connection with the issue or sale of any Notes in circumstances in which Section 21(1) of the FSMA does not apply to the Issuer; and

- (c) ***General compliance:***

it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to any Notes in, from or otherwise involving the United Kingdom.

Japan

The Notes have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended, the "FIEA"). Accordingly, each of the Dealers has represented and agreed, and each further Dealer appointed under the Programme will be required to represent and agree, that it has not, directly or indirectly, offered or sold and will not, directly or indirectly, offer or sell any Notes in Japan or to, or for the benefit of, a resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organised under the laws of Japan) or to others for re-offering or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident in Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, FIEA and other relevant laws and regulations of Japan.

Hong Kong

Each of the Dealers has represented and agreed, and each further Dealer appointed under the Programme will be required to represent and agree, that:

- (a) it has not offered or sold and will not offer or sell in Hong Kong, by means of any document, any Notes other than (i) to "**professional investors**" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong (the "**SFO**") and any rules made under the SFO; or (ii) in other circumstances which do not result in the document being a "**Prospectus**" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong (the "**C(WUMPO)**") or which do not constitute an offer to the public within the meaning of the C(WUMPO); and
- (b) it has not issued or had in its possession for the purposes of issue, and will not issue or have in its possession for the purposes of issue, whether in Hong Kong or elsewhere, any advertisement, invitation or document relating to the Notes, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to Notes which are or are intended to be disposed of only to persons outside Hong Kong or only to "**professional investors**" as defined in the SFO and any rules made under the SFO.

People's Republic of China

Each of the Dealers has represented and agreed, and each further Dealer appointed under the Programme will be required to represent and agree, that the Notes have not been and will not be offered or sold directly or indirectly within the People's Republic of China (for such purposes, not including Hong Kong and Macau Special Administrative Regions or Taiwan (the "**PRC**")). This Base Prospectus, the Notes and any material or information contained or incorporated by reference herein in relation to the Notes have not been, and will not be, submitted to or approved/verified by or registered with the China Securities Regulatory Commission ("**CSRC**") or other relevant governmental and regulatory authorities in the PRC pursuant to relevant laws and regulations and thus may not be supplied to the public in the PRC or used in connection with any offer for the subscription or sale of the Notes in the PRC. Neither this Base Prospectus nor any material or information contained or incorporated by reference herein constitutes an offer to sell or the solicitation of an offer to buy any securities in the PRC.

The Notes may only be offered or sold to PRC investors that are authorised to engage in the purchase of Notes of the type being offered or sold. PRC investors are responsible for obtaining all relevant government regulatory approvals/licences, verification and/or registrations themselves, including, but not limited to, any which may be required from the State Administration of Foreign Exchange, the CSRC, the China Banking Regulatory Commission, the China Insurance Regulatory Commission and other relevant regulatory bodies, and complying with all relevant PRC regulations, including, but not limited to, all relevant foreign exchange regulations and/or outbound investment regulations.

Singapore

Each Dealer has acknowledged, and each further Dealer appointed under the Programme will be required to acknowledge, that this Base Prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, each Dealer has represented and agreed, and each further Dealer appointed under the Programme will be required to represent and agree, that it has not offered or sold any Notes or caused any Notes to be made the subject of an invitation for subscription or purchase and it will not offer or sell any Notes

or cause any Notes to be made the subject of an invitation for subscription or purchase, and it has not circulated or distributed, nor will it circulate or distribute, this Base Prospectus or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of any Notes, whether directly or indirectly, to any person in Singapore other than (i) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time (the "SFA")) pursuant to Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the Notes are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities or securities based derivative contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the Notes pursuant to an offer made under Section 275 of the SFA, except:

- i. to an institutional investor or to a relevant person or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- ii. where no consideration is or will be given for the transfer;
- iii. where the transfer is by operation of law;
- iv. as specified in Section 276(7) of the SFA; or
- v. as specified in Regulation 37A of the Securities and Futures (Offers of Investment) (Securities and Securities-based Derivatives Contracts) Regulations 2018.

General

Each Dealer has represented, warranted and agreed, and each further Dealer appointed under the Programme will be required to represent, warrant and agree, that it has complied and will comply with all applicable laws and regulations in each country or jurisdiction in or from which it purchases, offers, sells or delivers Notes or possesses, distributes or publishes this Base Prospectus or any Final Terms or any related offering material, in all cases at its own expense. Other persons into whose hands this Base Prospectus or any Final Terms comes are required by the Issuer and the Dealers to comply with all applicable laws and regulations in each country or jurisdiction in or from which they purchase, offer, sell or deliver Notes or possess, distribute or publish this Base Prospectus or any Final Terms or any related offering material, in all cases at their own expense.

The Dealer Agreement provides that the Dealers shall not be bound by any of the restrictions relating to any specific jurisdiction (set out above) to the extent that such restrictions shall, as a result of change(s) or change(s) in official interpretation, after the date hereof, of applicable laws and regulations, no longer be applicable but without prejudice to the obligations of the Dealers described in the paragraph headed "*General*" above.

Selling restrictions may be supplemented or modified with the agreement of the Issuer. Any such supplement or modification may be set out in the relevant Final Terms (in the case of a supplement or modification relevant only to a particular Tranche of Notes) or in a supplement to this Base Prospectus.

Certain of the Dealers and their affiliates have engaged, and may in the future engage, in investment banking and/or commercial banking transactions with, and may perform services for, the Issuer and their affiliates in the ordinary course of business. In addition, in the ordinary course of their business activities, the Dealers and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or

instruments of the Issuer or Issuer's affiliates. Certain of the Dealers or their affiliates that have a lending relationship with the Issuer routinely hedge their credit exposure to the Issuer consistent with their customary risk management policies. Typically, such Dealers and their affiliates would hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in securities, including potentially the Notes issued under the Programme. Any such short positions could adversely affect future trading prices of Notes issued under the Programme. The Dealers and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

GENERAL INFORMATION

Authorisation

The establishment and most recent update of the Programme was authorised by the Board of Directors of the Issuer on 24 July 2007 and 17 May 2018. The Issuer has obtained or will obtain from time to time all necessary consents, approvals and authorisations in connection with the issue and performance of the Notes.

Legal and Arbitration Proceedings

Save as disclosed in Note 29 to the Issuer's consolidated financial statements for the year ended 31 December 2018 on pages 194 to 199 (inclusive) of the Issuer's Annual Report and Form 20-F Information 2018 and in Note 5 on pages 53 to 54 (inclusive) of the Issuer's Q1 Results dated 26 April 2019, which have been incorporated by reference into this Base Prospectus, there are no governmental, legal or arbitration proceedings, (including any such proceedings which are pending or threatened, of which the Issuer is aware), which may have, or have had during the 12 months prior to the date of this Base Prospectus, a significant effect on the financial position or profitability of the Issuer and its Subsidiaries.

Significant/Material Change

Since 31 December 2018 there has been no material adverse change in the prospects of the Issuer and since 31 March 2019 there has been no significant change in the financial or trading position of the Group.

Auditors

The consolidated financial statements of the Issuer as at and for the year ended 31 December 2017 and 31 December 2018 were audited without qualification by PricewaterhouseCoopers LLP, independent registered accounting firm.

Documents on Display

Copies of the following documents may be inspected during normal business hours at the specified offices of the Principal Paying Agent in London for 12 months from the date of this Base Prospectus:

- (a) the Memorandum and Articles of Association of the Issuer;
- (b) the unaudited interim financial statements of the Issuer for the 3 months ended 31 March 2019;
- (c) the audited consolidated financial statements of the Issuer as at and for the years ended 31 December 2017 and 31 December 2018;
- (d) the Agency Agreement;
- (e) the Trust Deed;
- (f) the Programme Manual (which contains the forms of the Notes in global and definitive form); and
- (g) the Issuer-ICSDs Agreement.

Clearing of the Notes

The Notes have been accepted for clearance through Euroclear and Clearstream and, in the case of Renminbi Notes cleared through the CMU, the CMU. The appropriate common code and the International Securities Identification Number (ISIN), the Financial Instrument Short Name (FISN) and Classification of Financial Instruments (CFI) code (as applicable) in relation to the Notes of each Tranche will be specified in the relevant Final Terms.

Yield

The yield of each Tranche of Notes set out in the applicable Final Terms will be calculated as of the relevant issue date on an annual or semi-annual basis using the relevant issue price. It is not an indication of future yield.

LEI

The Legal Entity Identifier code of the Issuer is PY6ZZQWO2IZFZC3IOL08.

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